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Formaldehyde Health Effects

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Health effects literature primarily related to inhalation exposure to formaldehyde was collected, evaluated, tabulated, and summarized. Approximately 425 documents were collected from computerized and manual literature searches covering the period 1905-1981. Pharmacologists and an M.D. epidemiologist rated the documents according to their applicability to the study and their methodology. The approximately 110 documents considered useful for deriving a range of concern for human exposure to formaldehyde from automotive emissions were tabulated. The 145 pages of tables detail the results of acute, repeated dose, and chronic testing of mice, hamsters, rats, guinea pigs, rabbits, cats, pigs, dogs, monkeys, and humans as well as human occupational and epidemiological studies. Most of the documents evaluated are described in an annotated bibliography.

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Aldehydes	Epidemiology		
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For

Emission Control Technology Division
Office of Mobile Source Air Pollution Control
U.S. Environmental Protection Agency
2565 Plymouth Road
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Attn: Robert J. Garbe

PREFACE

This report on health effects of formaldehyde was prepared by Midwest Research Institute (MRI) as Task No. 5 under Contract No. 68-03-2928, "Health Effects Support for the Emission Control Technology Division," U.S. Environmental Protection Agency.

Health effects literature primarily related to inhalation exposures to formaldehyde has been collected, evaluated, tabulated, and summarized so that this report can be used to derive a range of concern for human exposure to formaldehyde from vehicular emissions to the air.

Task activities were coordinated by the project leader, Mrs. Bonnie L. Carson, Senior Chemist, and the co-task leader, Ms. Cecily M. Beall, Assistant Scientist. Documents were rated and summarized by senior pharmacologists Drs. Harry V. Ellis III and Betty L. Herndon, of MRI, and consultant epidemiologist Larry H. Baker, M.D., MRI consultant, who is an Associate Professor of Community Health at the University of Kansas Medical Center. Contributors to the tables and annotated bibliography included the above as well as Ms. Joy L. McCann, Assistant Scientist, and Ms. Eileen M. Horn, Junior Chemist. Ms. Carol Foret served as a literature aide. This study was performed under the general supervision of Dr. Edward W. Lawless, Head, Chemical Impact Assessment Section.

Mr. Robert J. Garbe was the project officer for the Emission Control Technology Division, U.S. Environmental Protection Agency, and Ms. Colleen DeMeyer served as Branch Technical Representative.

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SUMMARY

This summary is organized into the following sections: Goals and Methods, Bioassay Tests, Animal Exposure Studies, Human Exposure Studies, and Recommended Range of Concern.

GOALS AND METHODS

The purpose of this compilation of data on the health effects of inhalation exposures to formaldehyde (HCHO) is to assist the Emission Control Technology Division (ECTD) of the U.S. Environmental Protection Agency (EPA) to establish the ranges of exposure conditions that are of concern for HCHO in exhausts from vehicles equipped with catalytic converters, and to be able to advise automobile manufacturers thereof. The situations of particular concern are during malfunctions and during exposures in traffic jams, parking and home garages, and other situations where little dilution of the exhaust is expected before inhalation. Most of the report is, as directed by ECTD, in the form of tables based on the literature reviewed. Data from exposures at levels higher than those of primary concern are included because strictly relevant information was scarce and these related data might prove helpful in assessing health effects at lower levels. This report focuses on the noncarcinogenic effects of formaldehyde rather than on its carcinogenicity to humans. The latter is an unresolved question of much importance, but regardless of whether it is a carcinogen, gaseous formaldehyde is strongly irritating to the human eye, nose, and throat and capable of causing allergic sensitization at the levels of concern identified herein.

Documents on inhalation effects of HCHO identified from manual and computerized literature searches were rated in a two-step process by the project pharmacologist and epidemiologist. First, the document received an A, B, C, or D rating according to its applicability for deriving a range of concern for HCHO in automobile emissions. Second, if the paper was not a low-rated, foreign language document,* a theoretical paper, a review, or a nontoxicology experimental paper, it received a numerical score based on itemized features that should be present in an ideal report. For the most part, only A- and B-rated documents were tabulated; but when any C- or D-rated studies involved low-level HCHO exposures, these were also tabulated. Blanks in the tables should be construed as denoting missing information in the documents.

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* Most foreign language articles rated C and D were usually not translated. Each foreign language document tentatively rated A or B from an English language abstract or brief examination of the paper was translated in sufficient degree to judge the experimental design and details. These papers were numerically scored from the translation.

BIOASSAY TESTS

Rabbit and rat tracheal tissue exposed very briefly to 0.6-125 mg HCHO/m^3 showed cessation of ciliary movement, with decreasing concentrations showing increasing time to ciliostasis. Exposure to 0.6 mg HCHO/m^3 caused ciliostasis within 2.5 min followed by recovery within 10-30 s after exposure stopped. All the other concentrations studied were above 3 mg HCHO/m^3, the threshold limit value.

ANIMAL EXPOSURE STUDIES

Animal exposure studies show that the animal organism can recover from moderately irritating doses of inhaled HCHO. However, there is a limit to this recovery, as shown by the progressively increasing time to recovery and the nasal cancers observed in rats and mice after long-term exposures to 7 and/or 17-19 mg HCHO/m^3, although not all studies increased tumor incidence in animals exposed to these levels.

Table S-1 summarizes studies of animal exposures to HCHO at concentrations up to 6 mg/m^3 (twice the threshold limit value).

There is no evidence of major differences in response to inhaled HCHO among the species tested. Moderate amounts of evidence show simple additivity with other irritants and with other air pollutants having different effects. The minimal adverse effects seem to be local irritation and subsequent tissue reactions, especially in the pulmonary system. Such adverse effects appear at levels at or above 1 mg/m^3, whether the animals were acutely or chronically exposed. In chronic studies, biochemical and inflammatory changes were reported at concentrations $\geq$ 0.035 mg/m^3. Rats exposed for only 8-12 wk to 0.012 mg/m^3 have also shown such changes.

HUMAN EXPOSURE STUDIES

Experimental Studies

Results of studies of acute human experimental exposure to HCHO are summarized in Table S-2. Moderate to severe irritation of the eye, nose, and throat was observed at concentrations of 1.25-17.3 mg/m^3. At ~ 1 mg HCHO/m^3, eye irritation is slight, but distortions occur in breathing and α-rhythms. The threshold for eye irritation is 0.2-0.25 mg/m^3. The reported odor thresholds range from 0.4 to ~ 0.1 mg/m^3.

Several studies found minimal effects at ~ 0.05-0.08 mg/m^3 (such as the electroencephalographic response to light). Exposures to 0.0024 to 0.029 mg/m^3 were said to cause effects ranging from mood changes to nervous system irritation (0.016 mg/m^3), thresholds of respiratory irritation (0.075 mg/m^3), and salivary action.

TABLE S-1. SUMMARY OF STUDIES OF ANIMAL EXPOSURES TO FORMALDEHYDE (HCHO) UP TO 6 mg/m^3*

Level (mg/m^3)	Time	Species	Effects
3.5-6	10 s	RBT	Threshold of olfactory sensitivity.
5	4 h	RAT	Decreased blood pressure; neutrophilia; eosinophilia; minor irritation to lungs, spleen, and marrow.
5-6	4 h/d, 20 d	RAT	Slight effect on neuromuscular system, slightly higher preimplantation mortality of embryos, development of offspring normal except for decreased spontaneous mobility.
4.6	90 d	RBT	Blood normal, inflammation in lungs.
4.6	90 d	DOG	Blood normal, inflammation in lungs.
4.6	90 d	MKY	Blood normal, inflammation in lungs.
2-4.6	53-90 d	GPG	No deaths; slight cholinesterase and leukocyte effects; inflammation in lung, heart, and kidneys. Allergic effects appeared at 14 d.
0.7-4.5	45-90 d	RAT	Lower body weight; slight inflammation of lungs, heart, and kidneys; and decreased DNA-ase activity of liver. Change in chronaxy ratio of antagonistic muscles; mild biochemical changes in brain, liver, kidneys, and blood. In lungs, hyperemia, desquamation and proliferation of lymphohistiocytic elements.
1.6-3.8	10 min	MUS	Respiration rate decreased 26 to 53%, with or without prior exposure to HCHO.

---

* This level, which is twice the threshold limit value (TLV), was arbitrarily chosen.

(continued)

TABLE S-1 (continued)

Level (mg/m^3)	Time	Species	Effects
1-4	3 h/d, 4 d	MUS	Initial respiration rate decrease of 18 to 72% at beginning of each exposure. Some recovery during exposure, less each day.
3.75	22 h/d 7 d/wk 6 mo	RAT HAM MKY	Nasal discharge in MKY; decreased weight gain in RAT
2-3.5	10 s - 10 min	RBT	Disturbance in nervous system responses.
2.5	6 h	PIG	No change in lung function, but moderate morphologic changes, more so in dorsal than ventral section. Changes included desquamation, interstitial edema, emphysema, and atelectasis.
1-2	4 h	RAT	No effect.
1.25	22 h/d 7 d/wk 6 mo	RAT HAM MKY	Nasal discharge in MKY; no other effects.
1.0	8 wk	RAT	Significant changes in ascorbic acid, nucleic acids, DNA levels in females and fetuses. Length of pregnancy increased, number of fetuses decreased, no deformities. Histochemical changes in heart, liver, and kidneys of fetuses.
1.0	8 mo	RAT	No effect on body weight or blood chemistry for either first generation or exposed offspring. Offspring had some morphological changes in lungs after 8-mo exposure.

(continued)

TABLE S-1 (continued)

Level (mg/m^3)	Time	Species	Effects
0.69	10 min	MUS	Respiration rate decreased 14 to 16% with or without prior exposure to HCHO.
0.6-2.5	1-4 h	RAT	Depression of nasal sensory response, partial recovery within 1 h.
0.4-0.5	4 h/d, 19-20 d	RAT	No overall toxic effects, fetuses normal.
0.5	4-5 h/d, 4-6 mo	RAT	No effects on general health, minor changes in blood and urine parameters.
0.038-0.5	5-8 h/d, 21-28 d	GPG	No effect on general health, minor changes in blood and urine parameters, formation of antibodies.
0.06-0.39	1 h	GPG	Significant change in lung function, some recovery within 1 h post-exposure.
0.03-0.25	6 h	PIG	Change in lung function and slight lung inflammation.
0.25	22 h/d 7 d/wk 6 mo	RAT HAM MKY	No effect.
0.1	69-90 d	RAT	Signs of beginning damage to nasal mucosa. DNA-ase activity of liver increased; of spleen, decreased.
0.031-0.035	90-98 d	RAT	No effect on overall health, nervous system response slowed slightly, slight inflammation areas in lungs and liver.
0.035	3-8 h/d, 6 mo	RAT	No effect on general condition, changes in metabolic processes of liver, blood changes, and testicular biochemical changes. Decreased sperm mobility.

(continued)

TABLE S-1 (concluded)

Level (mg/m^3)	Time	Species	Effects
0.012	8-12 wk	RAT	No effect on overall health, nervous system slowed slightly, slight inflammation in areas of lungs. Biochemical changes in livers of females and fetuses, increased length of pregnancy, decreased number of fetuses, no deformities. Histochemical changes in heart and kidneys of fetuses.
0.011	7-8 h/d, 21-30 d	GPG	Blood unaffected, phagocytic activity increased, formation of antibodies. When stressed 2 mo later by hypoxia, immune response and phagocytic activity adversely affected.

TABLE S-2. SUMMARY OF ACUTE HUMAN EXPERIMENTAL EXPOSURE TO FORMALDEHYDE.

Level (mg/m^3)	Effects
9.6 - 17.3	Irritation of the mucous membranes of the eyes, nose, and upper respiratory tract.
5.0 - 6.25	Moderate to severe eye irritation in most subjects, some nasal and throat irritation.
3.75-4.0	Moderate to severe eye irritation and throat irritation initially. Some adaptation by 30 min.
2.5	Moderate to severe eye irritation in some subjects; some nose and throat irritation.
2.0	Slight, insignificant changes in airway resistance; decreased nasal mucus flow rate; slight discomfort, with some acclimatization; no change in performance tests.
1.71	Decreased sensitivity to light in all subjects.
1.25	A few subjects experienced moderate to severe eye irritation; generally zero to moderate eye, nose, and throat irritation; lowest concentration at which the odor was recognized.
1.0	Slight, insignificant changes in airway resistance; slight discomfort in all subjects; no change in performance tests.
0.95 - 1.0	Slight irritation of the eyes and upper respitory tract; odor perceived; some changes in breathing rhythm and α-rhythms.
0.53	Threshold value for effect on electrical activity of the human brain.
0.5	Slight, insignificant changes in airway resistance; decreased nasal mucus flow rate; very slight discomfort in all subjects; no change in performance tests.
0.3 - 0.4	Odor perceived; change in bioelectric skin potential; delay in adaptation to darkness.

(continued)

TABLE S-2 (concluded)

Level (mg/m³)	Effects
0.3	Slight, insignificant changes in airway resistance; decreased nasal mucus flow rate; slight subjective discomfort in 3/15 subjects; no change in performance tests.
0.2 - 0.25	Threshold for eye irritation; increased sensitivity to light.
0.08 - 0.098	Minimum detectable odor level for some; threshold for eliciting reflex activity on optical chronaxy and dark adaptation.
0.07 - 0.077	Odor threshold for ~ 50% of the subjects; subthreshold level for effect on optical chronaxy and rheobase.
0.062 - 0.065	Odor threshold for 4/18, subthreshold for others.
0.05 - 0.054	Subthreshold value for odor detection; threshold value for EEG changes following flashing light.
0.04 - 0.046	Changes in the electrocortical conditioned reflex study; subthreshold value for EEG changes following flashing light.
0.035	Subthreshold value for the electrocortical conditioned reflex study.
0.029	Threshold of salivary action.
0.016	Threshold of irritation of the nervous system.
0.0024	Threshold of effect on the mood of human subjects.

Environmental Exposures

The occupational and epidemiological studies of HCHO exposures are summarized in Table S-3. Occupational studies were generally of a rather low quality, being confounded by exposure to other agents with similar irritating effects and having poor or no controls. Mucous membrane irritation was observed in occupational exposures to concentrations as low as 0.035-0.48 mg HCHO/m^3. Occupational studies are in progress, as described in Appendix A, with mortuary workers and histotechnologists who can have cutaneous as well as inhalation exposure. Definitive results are not yet available.

Most of the epidemiological studies and other reports of HCHO exposures of the general public are defective due to poor or no controls, selection bias, or lack of measurements of HCHO concentrations. Eye and upper respiratory tract irritation were reported at levels as low as 0.211 mg HCHO/m^3.

RECOMMENDED RANGE OF CONCERN

Human studies indicate that the range of concern in long-term or acute exposures to HCHO should be 0.06 (the lowest reported odor threshold) or 0.2 (the threshold for eye irritation) to $\sim$ 1 mg/m^3 (where slight eye irritation and other minor disturbances occur). If animal studies could be directly extrapolated to humans, the lower limit of the range of concern might be extended to values as low as 0.01-0.04 mg HCHO/m^3.

The value of 0.2 mg/m^3 may be the most defensible choice since both nonsmoking and smoking humans sometimes contain HCHO in the breath at levels as high as $\sim$ 0.1 mg/m^3, HCHO being a normal metabolite and a metabolite of exogenous substances. This value is frequently the maximum value reported for urban polluted air. However, authorities in the USSR have promulgated a standard of 0.01 mg/m^3 for HCHO in outdoor air, which is an order of magnitude lower than these values.

TABLE S-3. SUMMARY OF OCCUPATIONAL AND EPIDEMIOLOGICAL STUDIES OF EXPOSURES TO FORMALDEHYDE

Level (mg/m^3)	Exposure Time	Table	Effects
0.06-12.5		V-2	Residents of homes with urea-HCHO (UF) foam insulation: eye irritation and conjunctivitis, nose and throat irritation, respiratory symptoms, dizziness, nausea, drowsiness, memory lapse, headache, coughing, sneezing, fatigue, aches, rash, and skin growths.
0.11-6.58		V-1	Embalmers: eye and nose burns, sneezing, coughing, headaches, sinus, asthma, dermatitis.
≧ 6.25	8 mo	V-2	Children in a school where HCHO was present complained of burning eyes, abdominal pain, eye pain, nausea, vomiting, thirst, and apathy.
1.5-4.5	64% worked ≧ 10 y	V-1	Textile workers: increases in various menstrual disorders, inflammatory genital disease, primary and secondary sterility, maternal problems during pregnancy and delivery, and decreased neonatal weight.
0.38-3.88	≦ 6 mo	V-2	Employees and customers in a shopping center: eye (occasional lacrimation), nose, and throat irritation.
0.04-1.76 and wood dust	avg. 5.9 y	V-1	Employees in wood processing plant. Those exposed to higher levels performed visual tests less quickly and efficiently both before and after work than the lower-exposure group. Headache, eye irritation, fatigue; complaints less frequent in the highest exposure group.
0.25-1.25		V-2	Residents of homes with HCHO present: eye, nose, and throat irritation most frequent in adults. Coughing, wheezing, and skin rash most frequent in < 13-y-olds.

(continued)

TABLE S-3 (concluded)

Level (mg/m^3)	Exposure Time	Table	Effects
0.1-1.21		V-2	Teachers and students in school with HCHO present: headache, lack of concentration, dizziness, nausea, and respiratory tract irritation.
0-0.98	1-40 mo	V-2	Residents of homes with UF insulation: burning or tearing of eyes, runny nose, wheezing or breathing difficulty, headache, sleeping problems, and skin rash.
0.17-0.85	< 10- > 20 y	V-1	Sales persons in fabric shops. Mucus discharge, sleep disturbance, pains in the heart, angina, and nausea. Head pain, dizziness, irritation, stomach pains, and skin rash most common in the group with shorter employment. Cough, tickling in the nasopharynx, catarrh, poor appetite, and pains in the joints and small of the back more common in the group with longer employment.
0.25-0.75		V-2	Residents of apartment building where HCHO was present: burning eyes, lacrimation, and coughing.
0.05-0.7	56% worked ≧ 10 y	V-1	Inspectors in textile warehouses: various menstrual disorders; increased inflammatory genital disease, primary sterility, and problems during birth; decreased neonatal weights.
0.035-0.48	≤ 1 y ?	V-1	Garment factory workers: cutaneous and mucous membrane irritation.
0.211		V-2	Eye and upper respiratory tract irritation was reported by some of the residents living near a formalin-producing plant.
0.08-0.13		V-2	No complaints by residents of an apartment building. No complaints or increased absenteeism in children in a school where HCHO was present.

SECTION I

INTRODUCTION

This report was compiled as the fifth of several tasks under Contract No. 68-03-2928, "Health Effects Support for the Emission Control Technology Division (U.S. Environmental Protection Agency, Ann Arbor, Michigan)." The goal of the project is to evaluate health effects literature on specific compounds emitted from automobiles equipped with emission-control devices (specifically catalytic converters), not for the purpose of creating a criteria document but to identify a range of concern or a no-observable-effect level for each compound to serve as guidance to automobile manufacturers in their development of future emission-control devices.

The present report was meant to be largely a series of charts or tables of pertinent data with the tests logically ordered according to exposure levels. The narrative summary was not meant to describe each paper in detail. There are admittedly some disadvantages in not doing so; e.g., some of the gradations in effect that the authors of a particular paper observed may be diluted or lost when the details are spread throughout an exceptionally large table, or between several tables. Papers described in a largely narrative fashion, however, often are difficult to compare. Results that appear within their source paper to be quite definitive may appear less so or even anomalous when juxtaposed in tabular format with other results from similar studies. Hence, the present format was designed to facilitate comparisons.

Literature related to health effects of inhaled formaldehyde (HCHO) was collected mainly by computer searches of TOXLINE and TOXBACK and manual searches through several major review documents. Approximately 425 papers and other documents were evaluated, of which approximately 110 contained original data suitable for tabulation.

Experimental animal and human exposure studies and bioassay studies were evaluated and summarized by senior Ph.D. pharmacologists. Occupational and general public exposures were rated by an epidemiologist with an M.D. degree. Figure I-1 is the form used for rating documents by the project pharmacologist and epidemiologist. Each document was rated in a two-step procedure according to the applicability of its subject matter and to the quality of the experimental methodology. The letter assigned in rating the document A, B, C, or D was derived from the corresponding lower case letters under item 7 in Figure I-1. Thus, a study was rated A if it directly applies to or assists in establishing a range of concern for exposure to HCHO. The second part of the rating is the methodology score. The document reviewer checked off which score should be given for each of the first six items in Figure I-1, and the total was written at the top of the page along with the

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CHECK WHERE APPROPRIATE:	PAPER DEFECTIVE 0	PAPER IS SUB-STANDARD 1	STANDARD QUALITY 2	SUPERIOR PAPER 3
1. Do they state/limit the problem?				
2. Adequacy of sample				
3. Replicability				
4. Controls/control procedures				
5. Completeness and comprehensibility of results				
6. Validity of conclusions, interpretation of data				

7. Applicability to health effects of HCHO as guidance for establishing a range of concern for HCHO in automobile exhaust.

a. Clearly, directly applies/assists in establishing a range of concern.

b. Research requires major inferences; potentially applicable.

c. Useful hints or suggestions; tentatively applicable.

d. Not directly applicable (peripheral useful information).

Figure I-1 - Form for Report Rating

letter that rated the paper's applicability. In some cases, such as reviews, theoretical papers, and low-rated foreign language documents, a paper may have received an applicability rating (generally C or D) but none on methodology.

Data, including the MRI-assigned rating, from the A-, B-, and some C- and D-rated papers were tabulated by senior and mid-level scientists. Information for each topic heading was carefully sought; so if blanks appear in the table, the reader can generally assume the data were not given. Information which was unclear in the original document but needed for tabulation is preceded in the tables by a qualifying word such as "apparently." Sometimes a group published several papers that described the same tests. To avoid redundancy, all pertinent papers were cited and the test was described as well as possible from all the papers' descriptions.

The final written summary of the tabulated data was also performed by a senior pharmacologist. This summary attempts to reflect objectively the scientific community's thought as a whole and does not reflect the tabular material by weight. The tables reflect the amount of data generated, and the summary puts the evaluated data in perspective with the overall scientific community's opinions.

The references are cited in an annotated bibliography that includes not only each document's rating but also a brief comment on its pertinence (or lack of same) to the study. English titles are given for foreign language documents and an abbreviation of the language is given in parentheses at the end of the citation.

The report is organized into the following chapters: II. Bioassay Tests, III. Experimental Animal Inhalation Exposures, IV. Experimental Human Inhalation Exposures, V. Epidemiology and Related Human Exposures, VI. Summary of Health Effects Information, and VII. Human Exposures to Formaldehyde and Recommendations for a Range of Concern. The Summary precedes the report, and the Annotated Bibliography follows it. Appendix A describes human studies in progress.

SECTION II

BIOASSAY TESTS

The area of concern for this task report is the effects of HCHO inhalation. For that reason, only bioassays dealing with gaseous HCHO and respiratory tissues are tabulated in this chapter. However, Chapter VI contains a discussion not only of these results but also of mutagenicity tests.

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TABLE II-1. RESPIRATORY TRACT BIOASSAYS

Compound and Concentration mg/m³ (ppm)	Relative Humidity/ Temperature	Preparation Exposed	Description of Tests and Duration	Results	Reference and Rating
HCHO 1.6-163 µg/mL (unclear if this was the level in air or solution)	37°C	Cell cultures of alveolar macrophages obtained by lavage of the lungs of lightly anesthetized rabbits.	Cell cultures in salt solutions were incubated with bacteria (*Staphylococcus albus*) and HCHO. Bacterial counts were made by standard agar pour-plate procedures at 0, 1.5, and 3 h. Decreased counts indicate phagocytic ability.	No effect on alveolar macrophage activity.	Green and Carolin (1967) D--
HCHO 22.5-125 (18-100)	30-31°C	Fresh (≤ 2.5 h) excised rabbit tracheal tissue.	Section was placed in a tissue chamber and HCHO gas added for 5-10 min at a flow rate similar to that in the trachea of a living rabbit. Ciliary activity was observed microscopically during and after exposure.	Five-minute exposure to 38 mg/m³ or 10-min exposure to 22.5 mg/m³ caused cessation of ciliary activity without recovery in air. Five-minute exposure to 75-125 mg/m³ caused cessation of ciliary activity without recovery in Ringer's solution.	Cralley (1942) C-10
HCHO 11.6-61.7		Rabbit tracheal sections.	HCHO from an air nebulizer was added to a moist, temperate chamber at the rate of 54 L/h, for a maximum of 60 min. Ciliary beating was monitored (method not given) during exposure, but no recovery period was included.	Ciliary activity stopped immediately after exposure to 61.7 mg/m³. Decreasing concentrations caused increasing time to ciliostasis (48 min for 11.6 mg/m³).	Dalhamn and Rosengren (1971) C-5
HCHO 27.5 (22)	34°C, 90-95%	Rat tracheas, apparently opened and exposed *in situ*.	Ciliary activity was continuously observed microscopically for < 10 min, with continuous gas flow over the tracheas.	Ciliary movement ceased in 10 s.	Dalhamn (1956) C-6
HCHO 12.5 (10)	34°C, 90-95%	Rat tracheas, apparently opened and exposed *in situ*.	Ciliary activity was continuously observed microscopically for < 10 min, with continuous gas flow over the tracheas.	Ciliary movement ceased in 30 s.	Dalhamn (1956) C-6

(continued)

TABLE II-1 (concluded)

Compound and Concentration mg/m^3 (ppm)	Relative Humidity/ Temperature	Preparation Exposed	Description of Tests and Duration	Results	Reference and Rating
HCHO 5	37°C	Excised rabbit tracheas opened longitudinally.	Tissue was exposed to 6 µg HCHO/ 12-s puffs (40 mL), ~ 1 min apart, for 8 puffs. The time for the ciliary transport of tracer particles (soot and lycopodium particles) a distance of 5 mm was measured.	The dose required per puff to produce a 50% inhibition of ciliary transport rate after 8 puffs was 6 µg/puff (150 mg/m^3). This contrasts with the 2 µg/ puff given as the HCHO level in cigarette smoke.	Kensler and Battista (1963) B-13
HCHO 3.75 (3)	34°C, 90-95%	Rat tracheas, apparently opened and exposed in situ.	Ciliary activity was continuously observed microscopically for < 10 min, with continuous gas flow over the tracheas.	Ciliary movement ceased in 50 s.	Dalhamn (1956) C-6
HCHO 0.6 (0.5)	34°C, 90-95%	Rat tracheas, apparently opened and exposed in situ.	Ciliary activity was continuously observed microscopically for < 10 min, with continuous gas flow over the tracheas, then for a short recovery period.	Ciliary movement ceased in 2.5 min. Beating began again 10-30 s after exposure stopped.	Dalhamn (1956) C-6

SECTION III

EXPERIMENTAL ANIMAL INHALATION EXPOSURES

The essential parameters of numerous animal inhalation exposure experiments are tabulated in this section. The primary organization of data is by species, in order of increasing weight (mice to monkeys in this case). Within a species, studies are divided by dosing duration: acute exposure (≦ 24 h), repeated exposure, and chronic exposure (> 90 d). A summary of the data for all species ordered by decreasing HCHO concentration is in Table III-17.

The tables have been grouped by species and arranged by decreasing HCHO concentration for the following reasons: (a) there were about 170 separate tests tabulated; (b) there are distinct differences in lung anatomy among the laboratory species used, and the differences seen in their relative responses may have been largely due to these anatomical differences; and (c) by putting the highest concentrations and worst effects first, one can more readily understand the significance of minor or less-severe changes occurring at lower levels.

The general rating system described in Figure I-1 was modified for assigning applicability ratings to the animal exposure documents. Those studies with data on chronic exposure or acute exposure with minimal effects were rated B. Studies with acute exposures and severe effects or any study with unusual endpoints not obviously important to respiratory exposure were rated C. Exposures which were confounded by the presence of other compounds, or were measured by very unusual endpoints of doubtful significance were rated D. The C- and D-rated studies were tabulated if the confounding compounds are also found in automotive exhaust, if HCHO was the primary toxicant, or if the HCHO level was low. No animal studies were rated A because of the controversy surrounding extrapolation of effects observed in animals to humans.

In the animal exposure tables in this section, the column headed "Total Length of Experiment" includes not only the total length of exposure to HCHO, but also any recovery time observed in the study. This recovery time was included to note the endurance or reversibility of the toxic effects.

Chapter VI contains a discussion of the animal exposure data.

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TABLE III-1. MICE--ACUTE EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 900		Inhalation chamber, 623-L	Mice, C3H strain	Not given	Not given	2 h, once	2 h	Death of animals from massive pulmonary hemorrhage and edema.	Horton et al. (1963) B-10
HCHO ~ 16.8 (13.4)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M	Served as own control	10 min, once	10 min	Respiration rate decreased 77.5%.	Kane and Alarie (1977) B-12
HCHO ~ 12.6 (10.1)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M	Served as own control	10 min once	10 min	Respiration rate decreased 73.7%.	Kane and Alarie (1977) B-12
HCHO ~ 12.16 (9.73) Acrolein ~ 20.63 (8.97)		Inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M		10 min, once	10 min,	Maximum decrease in respiratory rate was 74.4%.	Kane and Alarie (1978) B-10
HCHO ~ 9.88 (7.90)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M	Served as own control	10 min, once	10 min	Respiration rate decreased 65.6%.	Kane and Alarie (1977) B-12
HCHO ~ 8.96 (7.17) Acrolein ~ 1.68 (0.73)		Inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M		10 min, once	10 min	Maximum decrease in respiratory rate was 69.6%.	Kane and Alarie (1978) B-10

(continued)

TABLE III-1 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 5.61 (4.49) Acrolein ~ 18.31 (7.96)		Inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M		10 min, once	10 min	Maximum decrease in respiratory rate was 71.3%.	Kane and Alarie (1978) B-10
HCHO ~ 4.30 (3.44) Acrolein ~ 4.00 (1.74)		Inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M		10 min once	10 min	Maximum decrease in respiratory rate was 62.0%.	Kane and Alarie (1978) B-10
HCHO ~ 3.8 ± 0.35 (3.0±0.28)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	20 M (5 groups of 4 animals)	Served as own control	10 min, once	10 min	Decrease in respiratory rate of 54%.	Kane and Alarie (1977) B-12
HCHO ~ 3.8 (3)		Inhalation chamber Tracheal cannula inserted under anesthesia	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	? M	? M Controls had been anesthetized only	10 min, once	10 min	Respiration rate decreased 54% vs. 4.2% for controls.	Kane and Alarie (1977) B-12
HCHO ~ 3.50 (2.80)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M	Served as own control	10 min, once	10 min	Respiration rate decreased 51.5%.	Kane and Alarie (1977) B-12
HCHO ~ 3.13 (2.50) Acrolein ~ 4.72 (2.05)		Inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M		10 min, once	10 min	Maximum decrease in respiratory rate was 61.8%.	Kane and Alarie (1978) B-10

(continued)

TABLE III-1 (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 3.13 (2.50) Acrolein ~ 1.56 (0.68)		Inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M		10 min, once	10 min	Maximum decrease in respiratory rate was 52.8%.	Kane and Alarie (1978) B-10
HCHO ~ 1.89 (1.51)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M	Served as own control	10 min, once	10 min	Respiration rate decreased 41.0%.	Kane and Alarie (1977) B-12
HCHO ~ 1.78 (1.42) Acrolein ~ 4.30 (1.87)		Inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M		10 min, once	10 min	Maximum decrease in respiratory was 60.7%.	Kane and Alarie (1978) B-10
HCHO ~ 1.54 ± 0.24 (1.23 ± 0.19)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	36 M (9 groups of 4 animals)	Served as own control	10 min, once	10 min	Decrease in respiratory rate of 28%.	Kane and Alarie (1977) B-12
HCHO ~ 1.63 (1.30)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M	Served as own control	10 min, once	10 min	Respiration rate decreased 27.7%.	Kane and Alarie (1977) B-12
HCHO ~ 1.08 (0.86) Acrolein ~ 1.29 (0.56)		Inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M		10 min, once	10 min	Maximum decrease in respiratory rate was 41.4%.	Kane and Alarie (1978) B-10

(continued)

TABLE III-1 (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 0.99 (0.79) Acrolein ~ 18.15 (7.89)		Inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M		10 min, once	10 min	Maximum decrease in respiratory rate was 77.9%.	Kane and Alarie (1978) B-10
HCHO ~ 0.69 (0.55)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M	Served as own control	10 min, once	10 min	Respiration rate decreased 13.7%.	Kane and Alarie (1977) B-12
HCHO ~ 0.46 (0.37) Acrolein ~ 0.28 (0.12)		Inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M		10 min, once	10 min	Maximum decrease in respiratory rate was 20.2%.	Kane and Alarie (1978) B-10
HCHO ~ 0.41 (0.33) Acrolein ~ 0.85 (0.37)		Inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M		10 min, once	10 min	Maximum decrease in respiratory rate was 30.1%.	Kane and Alarie (1978) B-10

TABLE III-2. MICE--REPEATED DOSE EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 200		Inhalation chamber, 623-L	Mice, C3H strain	42	59	1 h/d, 3 d/wk	~ 25 d, 11 exposures	Exposures were stopped after 11 because of high number of deaths--15 animals died. Tracheobronchial epithelium of the lungs of 5 mice that died had atypical metaplasia and 7 had squamous-cell metaplasia. Of 35 lungs examined, 2 had no changes; 4, basal-cell hyperplasia; 8, stratification; 16, squamous-cell metaplasia; 5, atypical metaplasia, and 0, tumors. Majority of control animals showed no significant changes of lungs.	Horton et al. (1963) B-10
HCHO 140		Inhalation chamber, 623-L	Mice, C3H strain	Not given	Not given	2 h/d	4 d	No signs of substantial distress or loss of weight.	Horton et al. (1963) B-10
HCHO ~ 16.8 (13.4)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	8 M Exposed to 0.31 ppm HCHO 3 h/d for 3 d prior to this exposure.	Served as own control	10 min, once	10 min	Respiration rate decreased 77.8% with no evidence of prior exposure having caused sensitization when results from this test and similar one with no pre-exposure are compared.	Kane and Alarie (1977) B-12
HCHO ~ 12.6 (10.1)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	8 M Exposed to 0.31 ppm HCHO 3 h/d for 3 d prior to this exposure.	Served as own control	10 min, once	10 min	Respiration rate decreased 68.4% with no evidence of prior exposure having caused sensitization when results from this test and similar one with no pre-exposure are compared.	Kane and Alarie (1977) B-12

(continued)

TABLE III-2 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 9.88 (7.90)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	8 M Exposed to 0.31 ppm HCHO 3 h/d for 3 d prior to this exposure.	Served as own control	10 min, once	10 min	Respiration rate decreased 66.5% with no evidence of prior exposure having caused sensitization when results from this test and similar one with no pre-exposure are compared.	Kane and Alarie (1977) B-12
HCHO ~ 3.9 (3.1)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M	Served as own control	3 h/d	4 d	The respiration rate decreased during the first 10 min from 46% on d 1 to 72% on d 4. Rate increased somewhat over remainder of exposure period, but recovery was slower each d. On d 4 respiration rate at end of 3 h was still 50% less than control rate.	Kane and Alarie (1977) B-12
HCHO ~ 3.50 (2.80)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	8 M Exposed to 0.31 ppm HCHO 3 h/d for 3 d prior to this exposure.	Served as own control	10 min, once	10 min	Respiration rate decreased 49.4% with no evidence of prior exposure having caused sensitization when results from this test and similar one with no pre-exposure are compared.	Kane and Alarie (1977) B-12
HCHO ~ 1.89 (1.51)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	8 M Exposed to 0.31 ppm HCHO 3 h/d for 3 d prior to this exposure.	Served as own control	10 min, once	10 min	Respiration rate decreased 36.8% with no evidence of prior exposure having caused sensitization when results from this test and similar one with no pre-exposure are compared.	Kane and Alarie (1977) B-12

(continued)

TABLE III-2 (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 1.63 (1.30)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	8 M Exposed to 0.31 ppm HCHO 3 h/d for 3 d prior to this exposure.	Served as own control	10 min, once	10 min	Respiration rate decreased 26.4% with no evidence of prior exposure having caused sensitization when results from this test and similar one with no pre-exposure are compared.	Kane and Alarie (1977) B-12
HCHO ~ 1.3 (1.0)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	4 M	Served as own control	3 h/d	4 d	The respiration rate decreased during the first 10 min from 18% on d 1 to 38% on d 4. Rate gradually moved toward pre-exposure level over the 3-h exposure period. Each d recovery was slower than on the previous d.	Kane and Alarie (1977) B-12
HCHO ~ 0.69 (0.55)		Head only, 2.1-L inhalation chamber	Mice, Swiss-Webster, Specific Pathogen Free, 20-30 g	8 M Exposed to 0.31 ppm HCHO 3 h/d for 3 d prior to this exposure.	Served as own control	10 min, once	10 min	Respiration rate decreased 15.6% with no evidence of prior exposure having caused sensitization when results from this test and similar one with no pre-exposure are compared.	Kane and Alarie (1977) B-12

TABLE III-3. MICE--CHRONIC EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 100		Inhalation chamber, 623-L	Mice, C3H strain	60	59	1 h/d, 3 d/wk	35 wk	Animals tolerated exposure with avg. wt. rising normally. The tracheobronchial epithelia of 35 lung were examined and 4 had no changes; 10, basal-cell hyperplasia; 14, stratification; 6, squamous-cell metaplasia; and 0, atypical metaplasia or tumors. Extension of epithelial changes into major bronchi was infrequent and none in the smaller bronchi. Majority of control animals showed no significant changes of lungs.	Horton et al. (1963) B-10
HCHO 50, then raised to 150		Inhalation chamber, 623-L	Mice, C3H strain	60 36 (second phase)	59	1 h/d, 3 d/wk	35 wk at lower level, 33 wk at higher level.	Animals tolerated exposure with avg. wt. rising normally. Some basal-cell hyperplasia in 6 and stratification in 9 tracheobronchial epithelia of 23 lungs examined after first 35 wk of exposure. During second exposure period, 15 animals died, but none had squamous-cell tumors in lungs. The changes in epithelium began extending into the major bronchi during the second phase. Majority of control animals showed no significant changes of lungs.	Horton et al. (1963) B-10

(continued)

TABLE III-3 (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 19 (15)*	45 ± 5% 20-22°C	Hinners-type ininhalation chamber 12 air changes/h	Mice, B6C3F1	120 M 120 F ?	120 M 120 F ?	6 h/d 5 d/wk	24 mo	No tumors at 18 mo but two of 85 had developed squamous cell carcinomas of the nasal turbinates after 24 mo. Only spontaneous levels of cancer were found in other organs and tissues.	NIOSH/OSHA (1980) C-- Swenberg et al. (1980) B-15 Selikoff and Hammond (1981) C-- Anonymous (1981)
HCHO ~ 7.5 (6)	45 ± 5% 20-22°C	Hinners-type inhalation chamber 12 air changes/h	Mice, B6C3F1	120 M 120 F ?	120 M 120 F ?	6 h/d 5 d/wk	24 mo	No tumors.	NIOSH/OSHA (1980) C-- Swenberg et al. (1980) B-15 Selikoff and Hammond (1981) C--
HCHO 2.5 (2)	45 ± 5% 20-22°C	Hinners-type inhalation chamber 12 air changes/h	Mice, B6C3F1	120 M 120 F ?	120 M 120 F ?	6 h/d 5 d/wk	24 mo	No tumors.	NIOSH/OSHA (1980) C-- Swenberg et al. (1980) B-15 Selikoff and Hammond (1981) C--

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* At the CIIT Conference on November 20-21, 1980, Dr. Craig Barrow and Dr. James Swenberg of CIIT indicated that "because of a difference in behavioral pattern, the effective exposure in the mice was about half that for rats. Thus, the cancer incidence in mice at 15 ppm can be considered comparable to that of rats at 6 ppm." (CPSC, 1981).

TABLE III-4. HAMSTERS--ACUTE EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 712 (570)		Inhalation chamber, ~ 1 ft^3	Hamsters, Syrian golden, avg. 100 g	8 M & F	None	4 h, once	96 h; 6, 12, 24, 48, and 96 h after beginning, 2 animals were sacrificed.	No recruitment of polymorphonuclear leukocytes to airway cells. Cytotoxic effects on airway cells; 34-100% of trachea cells and 5% of bronchial cells were exfoliated.	Kilburn and McKenzie (1978) B-11
HCHO ~ 525 (420) Carbon 21		Inhalation chamber, ~ 1 ft^3	Hamsters, Syrian golden, avg. 100 g	8 M & F	12 M & F Exposed to 1,032 mg C/m^3 alone. Animals sacrificed and examined 6, 12, 24, and 48 h after beginning exposure.	4 h, once	48 h;, 6, 12, 24, and 48 h after beginning, 2 animals were sacrificed.	Recruitment of polymorphonuclear leukocytes to airway cells; no recruitment in controls. Limited cytotoxic effect on trachea cells; 7% were exfoliated.	Kilburn and McKenzie (1978) B-11

(continued)

TABLE III-4 (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 250-313 (200-250) Carbon 700 (Carbon coated with HCHO.)		Inhalation chamber, ~ 1 ft³	Hamsters, Syrian golden, avg. 100 g	6 M & F	12 M & F Exposed to 1,032 mg C/m³ alone. Animals sacririficed and examined 6, 12, 24, and 48 h after beginning exposure.	4 h, once	24 h; 6, 12, 24, and 48 h after beginning, 2 animals were sacrificed.	Recruitment of polymorphonuclear leukocytes to airway cells, no recruitment in controls. Cytotoxic effect to airway cells, especially exfoliation of tracheal and bronchial cells.	Kilburn and McKenzie (1978) B-11
HCHO ~ 258 (206) Carbon 567 (Carbon coated with HCHO.)		Inhalation chamber, ~ 1 ft³	Hamsters, Syrian golden, avg. 100 g	7 M & F	12 M & F Exposed to 1,032 mg C/m³ alone. Animals sacrificed and examined 6, 12, 24, and 48 h after beginning exposure.	4 h, once	48 h; 6, 12, 24, and 48 h after beginning, 1-2 animals were sacrificed.	Recruitment of polymorphonuclear leukocytes to airway cells; no recruitment in controls. Cytotoxic effects to airway cells; 75-100% of tracheal cells and ≦ 25% of bronchial cells were exfoliated.	Kilburn and McKenzie (1978) B-11

(continued)

TABLE III-4 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 12.5 (10)		Inhalaation chamber	Syrian golden hamsters	? M	? M	5 h	4 d	No increase in 3H-thymidine incorporation (measuring cell proliferation) in nasal turbinates or tracheal epithelium, indicating little cell damage and subsequent repair.	Dalbey (1981) B12
HCHO ~ 8 (6)		Inhalation chamber, ~ 1 ft^3	Hamsters, Syrian golden, avg. 100 g	12 M & F	None	4 h, once	96 h; 6, 12, 24, 48 and 96 h after begining, 2 animals were sacrificed.	No recruitment of polymorphonuclear leukocytes to airway cells. Cytotoxic effects on airway cells; ~ 20% of tracheal and bronchial cells were exfoliated.	Kilburn and McKenzie (1978) B-11
HCHO ~ 8 (6) Carbon 805 (Carbon coated with HCHO.)		Inhalation chamber, ~ 1 ft^3	Hamsters, Syrian golden, avg. 100 g	12 M & F	12 M & F Exposed to 1,032 mg C/m^3 alone. Animals sacrificed and examined 6, 12, 24, and 48 h after beginning exposure.	4 h, once	62 d, 1, 2, 4, 8, 16, 32, and 64 d after beginning, 1-2 animals were sacrificed.	Recruitment of polymorphonuclear leukocytes to airway cells, no recruitment in controls. Cytotoxic effect to airway cells; 18-36% of tracheal cells but only 2% of bronchial cells were exfoliated.	Kilburn and McKenzie (1978) B-11

(continued)

TABLE III-4 (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 4 (3) Carbon 131		Inhalation chamber, ~ 1 ft^3	Hamsters, Syrian golden, avg. 100 g	6 M & F	12 M & F Exposed to 1,032 mg C/m^3 alone. Animals sacrificed and examined 6, 12, 24, and 48 h after beginning exposure.	4 h, once	48 h; 6, 12, 24, and 48 h after beginning, 1-2 animals were sacrificed.	Recruitment of polymorphonuclear leukocytes to airway cells, no recruitment in controls. Cytotoxic effect to airway cells; 75-100% of tracheal cells and 5% of bronchial cells were exfoliated.	Kilburn and McKenzie (1978) B-11

TABLE III-5. HAMSTERS--REPEATED DOSE AND CHRONIC EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 312.5 (250)			Hamsters, Syrian golden, 3 mo	34	5	1 h/d 1-15 exposures	5 animals killed 2 d after 1, 2, 5, and 15th exposure, 3 animals killed 1st, 2nd, and 6th wk after last exposure.	Histologic and cytologic changes in tracheobronchial epithelium such as the appearance of very pleomorphic, large, poorly differentiated squamous cells with abnormal polylobulated nuclei. All changes were reversible as no abnormalities were observed in animals killed 2 or 6 wk after exposure ended.	Schreiber et al. (1979) C-8
HCHO 62.5 (50)		Inhalation chamber	Syrian golden hamsters	? M	132 M	once/week 17 wk	17 wk	No toxicity to nasal epithelium.	Dalbey (1981) B-12
HCHO 31.2 (25)		Inhalation chamber	Syrian golden hamsters	? M	? M	5 h, on days 1 and 7	11 d	Increased 3H-thymidine incorporation (measuring cell proliferation) for several days, indicating cell damage and repair; greater in nasal turbinates than trachea. Less incorporation after second exposure, indicating possible adaptation.	Dalbey (1981) B-12
HCHO 12.5 (10)		Cages in a 1.5 m³ inhalation chamber	Syrian golden hamsters	88 M	132 M	5 d/wk, "lifetime" (10-26 mo)	"Lifetime" (10-26 mo)	Decreased survival time. No respiratory tract tumors. Little evidence of toxicity in nasal epithelium.	Dalbey (1981) B-12
HCHO 3.75 (3)		Inhalation	Hamsters	10	10	22/h/d 7 d/wk 6 mo	6 mo	No adverse effects noted during exposure.	Clary (1980) B--
HCHO ~ 3 (2)		Inhalation chamber, ~ 1 ft³	Hamsters, Syrian golden, avg. 100 g	Not given	Not given	4 h, every 3rd d for 6-10 expos-	18-30 d	Early exfoliation of 50% of tracheal cells and changes in epithelium but no increase in polymorphonuclear leukocytes in airway cells over controls.	Kilburn and McKenzie (1978) B-11

(continued)

TABLE III-5 (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 1.25 (1)		Inhalation	Hamsters	10	10	22 h/d 7 d/wk	6 mo	No adverse effects noted during exposure or on pathological evaluation.	Clary (1980) B--
HCHO 0.25 (0.2)		Inhalation	Hamsters	10	10	22 h/d 7 d/wk	6 mo	No adverse effects noted while exposed or on pathological evaluation	Clary (1980) B--

TABLE III-6. RATS--ACUTE EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 600-1,700		Inhalation chamber	Rats	72	None	30 min	3 wk	LD_{50} was 1,000 mg/m^3. First deaths occurred between 6 and 24 h after exposure and continued over 3 wk. Total mortality 49 of 72. Upon exposure, animals became listless, showed lacrimation, secretion from nose, and difficulty breathing. Hyperemia of lungs, liver, and kidneys as well as bronchitis and edema of lungs. The same symptoms, but less pronounced, occurred after s.c. injection of 300 to 640 mg HCHO/kg.	Skog (1950) B-10
HCHO 63		Inhalation chamber	Albino rats, 180-240 g	10-12 M	10-12 M	Not given (4 h?)	Not given (4 h?)	The acceptable limit as to general toxic effect as measured by increase in the alanine aminotransferase activity.	Nagornyi et al. (1979) B-9
HCHO ~ 43.7 (35.0)		Inhalation chamber, airflow 2 ft^3/min	Rats, Sprague-Dawley, 200-300 g	8 M	8 M	18 h, once		Slight insignificant increase in wt. of liver and adrenals. Significant increase in alkaline phosphatase activity of liver.	Murphy et al. (1964) C-8
HCHO ~ 25 (20)		Inhalation chamber	Rats, Sprague-Dawley, 12-13 wk	10 M	? M	24 h, once	24 h intact animal exposure; cells--7 d in culture.	Pulmonary alveolar macrophage cells were collected from rats and cultured, then challenged with polystyrene latex spheres. Cells from exposed rats had decreased phagocytic activity and < 0.5 the total sphere uptake of the controls. Cells exhibited significantly increased adhesion to culture surface compared to controls.	Katz and Laskin (1977) C-7

(continued)

TABLE III-6 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 18		Inhalation chamber	Albino rats, 180-240 g	10-12 M	10-12 M	Not given	Not given	The acceptable limit as to general toxic effect as measured by reduction of O_2 uptake.	Nagornyi et al. (1979) B-9
HCHO ~ 12.5 (10)		Inhalation chamber	Rats, Sprague-Dawley, 12-13 wk	10 M	? M	24 h, once	24 h intact exposure; cells--7 d in culture	Pulmonary alveolar macrophage cells were collected from rats and cultured, then challenged with polystyrene latex spheres. Cells from exposed rats initially had increased phagocytic activity but were similar to controls in total sphere uptake. Cells exhibited significantly increased adhesion to culture surface compared to controls.	Katz and Laskin (1977) C-7
HCHO 5		Inhalation chamber	Rats	20 ?	20 ?	4 h ?		Decreased blood pressure, neutrophilia (with toxic granulations in the neutrophils), shift to the left of the differential white blood cell counts, and eosinophilia (expressed most on the following days with the appearance of juvenile forms and binucleated lymphocytes) were observed immediately after exposure. Signs of minor irritation of the lungs, spleen, and marrow.	Zaeva et al. (1968) B-5

(continued)

TABLE III-6 (concluded)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 0.6-3.2 (0.5-2.5)		Nose mask, breathing through cannula in trachea, second cannula allowed HCHO to be circulated through nasal cavity.	Rats, Sprague-Dawley, 250-400 g	3 M	Served as own control	2 min/ exposure, 4-7 min between exposures, ~ 16 exposures for 3 animals.	≤ 2.3 h	Decrease in nasal sensory response with increased concentration.	Kulle and Copper (1975) C-11
HCHO ~ 0.6-2.5 (0.5-2.0)		Nose mask, breathing through cannula in trachea, second cannula allowed HCHO to be circulated through nasal cavity.	Rats,~ Sprague-Dawley, 250-400 g	10 M	Served as own control	1 h/exposure, test between exposures with amyl alcohol to test nerve response. Up to 4 1-h exposures with some of the test animals.	≥ 4 h + 1 h in air	Exposure to HCHO consistently produced significant depression of amyl alcohol response of nasal nerves. Depression of nasal sensory response progressed with increased HCHO exposure. Partial recovery of sensory response upon exposure to air only for 1 h.	Kulle and Copper (1975) C-11
HCHO 1-2		Inhalation	Rats		4 h			No functional or organic changes detected.	Zaeva et al. (1968) B-5

TABLE III-7. RATS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 50-100		Inhalation	Rats			40 d; unclear if exposure was continuous or intermittent	40 d	Development of fairly extensive intoxication. HCHO levels in the blood reached 4.8 mg% (control level was 1 mg%).	Zaeva et al. (1968) B-5
HCHO 20	Not given	Inhalation chamber	Albino rats, 130-140 g	20 M 10 of each group received a synthetic diet with 18% protein (Group 1) and the other 10 of each group received an isocaloric diet enriched with 5 mg lipoamide/kg (Group 2). Rats maintained on synthetic diets for 2 wk before start of inhalation exposures.	20 M	3 h/d, 6 wk	≥ 8 wk	Group 1 showed aggressiveness, weighed 80% less than Group 2, and showed a significant increase in the duration of alcohol and hexobarbital narcosis. The protective effect of lipoamide appeared to be due to its activation of liver microsomal enzymes participating in the oxidative destruction of these narcotics. Group 1 also had a 6 ± 0.8% lower total serum protein content, lower albumin, higher gamma-globulins, and lower serum SH groups. Group 1 rats showed dystrophic and necrotic changes in the liver cells that were not apparent in the rats protected by lipoamide. Lower levels of general and reduced ascorbic acid and higher levels of its oxidized form were observed in the livers of the unprotected rats. The 1979 abstract may indicate a different study: rats protected by 32% protein in the diet compared to those receiving 18% protein showed normal protein metabolism. This abstract also does not give the frequency of exposures.	Goloshchapov and Agranovskii (1976) C-11 Goloshchapov (1979) C-5

(continued)

TABLE III-7 (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 15			Albino rats, no specific strain	M; No. not given	M; No. not given	Continuous	≥ 50 h	The time until the increase in leukocyte no. was 129% that of controls was 15 h. Time until decrease in cholinesterase activity was 72% that of controls was 50 h.	Ostapovich (1975) C-6
HCHO 10.1 ± 2 (8.07 ± 1.62)	60% 23°C	Inhalation	Rats, Specific Pathogenic Free, 32-40 d	25 M	25 M	Continuous	2 mo	Sneezing and nasal discharge from 1st day of exposure, yellow coloration of fur, and 2 had serous discharge in eyes. Significantly lower body weight and relative liver weight than controls. Increased pulmonary macrophages, lymphocytes, and polynuclear cells. Reduced phagocytic activity, which suggested increase in number of small-sized macrophages.	Dubreuil et al. (1976) B-10
HCHO 7			Albino rats, no specific strain	M; No. not given	M; No. not given	Continuous	≥ 168 h (7 d)	The time until the increase in leukocyte no. was 132% that of controls was 60 h. Time until decrease in cholinesterase activity was 70% that of controls was 168 h.	Ostapovich (1975) C-6
HCHO 6.0 ± 0.3		Inhalation chamber	Albino rats, 200-230 g (non-pregnant)	8-32 F	8-32 F	4 h/d	20 d	Changes reported in kidney functions--decrease in daily diuresis and concentration of chlorides in urine and increase in concentration of albumin in urine. Change in liver function indicated by decrease in excretion of hippuric acid in urine after a sodium benzoate load. No effects on weight, nervous system function, or respiration.	Sanotskii et al. (1976) B-8

(continued)

TABLE III-7 (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 6.0 ± 0.3		Inhalation chamber	Albino rats, 200-230 g (pregnant)	8-32 F	8-32 F	4 h/d	20 d	Decrease in the concentration of hemoglobin in blood was the only reported effect. No effects on kidney function, weight, or respiration.	Sanotskii et al. (1976) B-8
HCHO ~ 5.7 ± 0.7 (4.55 ± 0.53)	60% 23°C	Inhalation chamber	Rats, Specific Pathogen Free, 32-40 d	25 M	25 M	Continuous	1.5 mo	Body weight slightly lower than controls, also yellow coloration of fur beginning from d 20.	Dubreuil et al. (1976) B-10
HCHO 5 ± 0.2		Inhalation chamber	Rats (pregnant)	~19 F	~19 F	4 h/d for 19 d	19 d for 15 rats; others through delivery and growth of offspring	Overall toxic effects observed were a lowering of the threshold of neuromuscular excitability, of rectal temperature, of hemoglobin in blood and a change in spontaneous mobility of post-experimental animals. Examination of females and fetuses at 20th d of pregnancy showed no deformities, but slightly higher preimplantation mortality of embryos. Development of offspring was normal except for a decrease in spontaneous mobility at one mo of age, which was also observed in female offspring at two mo. Some changes in peripheral blood composition were reported at 2 mo.*	Sheveleva (1971) B-11

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* The Formaldehyde Panel (Griesemer et al., 1980) felt the no. of animal per dose level and no. of dose levels were inadequate and skeletal and soft tissue analyses were missing. Still, the Panel felt there were indications HCHO affected reproductive potential.

(continued)

TABLE III-7 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 4.6 ± 0.4	50% 77 ± 2°F	Inhalation chamber (modified Rochester-type)	Rats, Long Evans and Sprague-Dawley	15 M&F	Not given	Continuous for 90 d (< 2.2% down time)	90 d	One death; others showed no signs of illness or toxicity. Hematologic values were normal, hearts and kidneys showed focal chronic inflammatory changes and lungs showed varying degrees of interstitial inflammation.	Coon et al. (1970) B-12
HCHO 3.9		Special 1 m^3 chambers	Albino rats 130-240 g	50 M	50 M	Continuous	60 d 6-10 rats sacrificed every 30 d.	The trend toward increasing DNA-ase activity of the liver seen at 0.1 and 0.7 mg HCHO/m^3 continued, but the decrease in spleen DNA-ase seen at these levels became a sharp increase at 3.9 mg/m^3. An increase in tissue DNA-ase agrees with reports of a decrease in tissue DNA seen in HCHO poisoning of rats.	Tiunov and Ivanova (1976) B-8)

(continued)

TABLE III-7 (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 3		100-L chambers; 30 L air + HCHO per min	Albino rats	15 M	15 M	Continuous (?) for 3 mo	3 mo	Definite structural and cytochemical shifts compared to the amygdaloid complexes of control rats are described. The effects on the olfactory analyzer are ascribed to the action of absorbed HCHO rather than to toxic irritation of the receptor regions. The relation of the chronaxy of the muscles-antagonists had become distorted by the end of the 2nd wk of poisoning. The distinct shortening of the chronaxy of the extensors was preserved until the end of poisoning. Significant lowering of cholinesterase activity occurred.	Bonashevskaya (1973) B-8
HCHO 3.0 ± 0.064		Inhalation chamber; 100-L with air flow of 30 L/min	Albino rats	25 M	25 M	Continuous	3 mo + 15-d recovery period	No effect on behavior or weight changes of animals. From end of 2nd wk chronaxial ratio of antagonistic muscles was inverted. Significant change in cholinesterase activity. In the lungs, a proliferation of lymphohistiocytic elements in the interalveolar walls and in the peribronchial and perivascular spaces, against a background of moderate hyperemia. Alveophages occurred in the alveolar lumini. Desquamation of the bronchial epithelium. Mild cytological and cytochemical alterations in the liver, kidneys, and brain. Adaptive responses from thyroid and adrenals.	Fel'dman and Bonashevskaya (1971) B-10

(continued)

TABLE III-7 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 2 ± 0.4 (1.60 ± 0.3)	60% 23°C	Inhalation chamber	Rats, Specific Pathogen Free, 32-40 d	25 M	25 M	Continuous	3 mo	No effect other than progressive yellowing of fur.	Dubreuil et al. (1976) B-10
HCHO 2			Albino rats, no specific strain	M No. not given	M No. not given	Continuous	≧ 1,758 h (73.25 d)	The time until the increase in leukocyte number was 133% that of controls was 456 h. Time until decrease in cholinesterase activity was 72% that of controls was 1,758 h.	Ostapovich (1975) C-6
HCHO 1.7 ± 0.3 (1.36 ± 0.20) Acrolein ~ 1.1 ± 0.3 (0.48 ± 0.12) Total aldehydes calcd. as HCHO ~ 22.1 ± 0.8 (17.7 ± 0.6) CO (≤ 20) Particulates 8.0 ± 0.6		Inhalation chamber	Rats, Wistar, 240 ± 22 g	20 M	20 M	6 d, 5 d/wk	5 wk	Animals were inactive during exposure period, preening increased, and fur became discolored. After exposures, animals were killed and brains analyzed. RNA and microsomal superoxide dismutase were significantly increased. Glutathione and lysosomal acid proteinase activity and glycosylation of protein in vitro were unchanged. NADPH-diaphorase activity was decreased significantly.	Zitting and Savolainen (1979) C-10
HCHO ~ 1.7 ± 0.3 (1.36 ± 0.20) Acrolein ~ 1.1 ± 0.3 (0.48 ± 0.12) Total aldehyde calcd. as HCHO ~ 22.1 ± 0.8 (17.7 ± 0.6) CO (≤ 20) Particulates 8.0 ± 0.6		Inhalation chamber	Rats, Wistar, 240 ± 22 g	20 M	20 M	6 h, 5 d/wk	3 wk	Same effects as after 5 wk except RNA and microsomal superoxide dismutase activity were unchanged.	Zitting and Savolainen (1979) C-10

(continued)

TABLE III-7 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 1.7 ± 0.3 (1.36 ± 0.20) Acrolein ~ 1.1 ± 0.3 (0.48 ± 0.12) Total aldehyde calcd. as HCHO ~ 22.1 ± 0.8 (17.7 ± 0.6) CO (≦ 20) Particulates 8.0 ± 0.6		Inhalation chamber	Rats, Wistar, 240 ± 22 g	20 M	20 M	6 h, 5 d/wk	2 wk	Same effects as after 5 wk except microsomal superoxide dismutase activity unchanged.	Zitting and Savolainen (1979) C-10
HCHO 1		100-L Chambers; 30 L air + HCHO per min	Albino rats	15 M	15 M	Continuous (?) for 3 mo	3 mo Not stated how long after end of poisoning the rats were killed by decapitation	A disturbance in the normal relation of the chronaxy of the muscles-antagonists was noted at the end of 2 mo. This parameter of poisoning did not attain the original level even after cessation of poisoning. No statistical change in cholinesterase activity.	Bonashevskaya (1973) B-8
HCHO 1.0 ± 0.03		Inhalation chamber, 100 L with air flow of 30 L/min	Albino rats	25 M	25 M	Continuous	3 mo + 15-d recovery period	No effect on behavior or weight changes of animals. End of 2nd mo, chronaxial ratio of antagonistic muscles became altered, recovery by 15th d. In the lungs, a proliferation of lymphohistiocytic elements in the interalveolar walls and in the peribronchial and perivascular spaces, against a background of moderate hyperemia. Alveophages occurred in the alveolar lumini. Desquamation of the bronchial epithelium. Mild cytological and cytochemical alterations in the liver, kidneys and brain. Adaptive responses from thyroid and adrenals.	Fel'dman and Bonashevskaya (1971) B-10

(continued)

TABLE III-7 (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 1.0		Inhalation chamber	Albino rats	10-12 F	10-12 F	Continuous 20 d; premating through pregnancy	~ 8 wk	Significant decrease in ascorbic acid in whole fetus, in female's liver, slight decrease in placenta. Significant increase in nucleic acids in both female's and fetus' liver. Significant decrease in DNA in female's and fetus' liver. Mean duration of pregnancy prolonged 14.5%. Avg. no. of fetuses 8.6 compared to 11.3 in controls. Significant decrease in fetal lung and liver wt.; significant increase in thymus, adrenals, and kidney wt. No external deformities, no inhibition of development of body systems, no macroscopic structural alterations in fetuses. Histochemical changes in fetuses included reduced glycogen content in the myocardium, accumulation of matter with a positive reaction to Schiff's reagent in the kidneys, and the presence of iron in Kupffer's cells. Some fetuses exhibited involution of lymphoid tissue indicating enhanced production of corticosteroid hormones in stress reactions, mild hypertrophy of Kupffer's cells, and numerous extramedullary myelopoietic centers in the liver.*	Pushkina and Gofmekler (1968) D-6 Gofmekler et al. (1968) D-6 Gofmekler (1968) D-5 Gofmekler and Bonashevskaya (1969) D-5

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* The Formaldehyde Panel (Griesemer et al., 1980) did not support the conclusions of Gofmekler et ai. (1968) that HCHO significantly inhibited the synthesis of nucleic acid; they also point out the data do not support reported avg. no. of fetuses/litter; different articles give different nos. of females and fetuses.

(continued)

TABLE III-7 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.7		Special 1 m^3 chambers	Albino rats, 130-240 g	50 M	50 M	Continuous	60 d (6-10 rats sacrificed every 30 d)	DNA-ase activity of the liver increased and of the spleen decreased. The effects were greater than those seen at 0.1 mg HCHO/m^3.	Tiunov and Ivanova (1976) B-8
HCHO $\leq$ 0.635 CO $\leq$ 5 $CO_2 \leq 0.005$ vol. % Benzene $\leq$ 20 for group 1 but 0.06-0.8 by day 10; 1.2-5 for Group 2. Concentrations were unchanged when fresh daily polymer was used but decreased when the same portion of polymer was used throughout the test		Gases were evolved from the heating of poly (methylphenylsiloxane) at 90°C in a 100-L chamber using either fresh daily 100 mL portions or the same 100 mL portion of the polymer. Air stream at 4 L/min	Albino rats, 180-270 g	10 F each Group 1 (same portion of polymer) Group 2 (fresh daily polymer)	10 F	4 h/d, 5 d/wk, 2 mo	$\geq$ 2 mo	No significant differences in general condition, summation threshold, O_2 consumption, morphological condition of the blood, and growth dynamics between the test animals and the controls.	Batulin et al. (1972) D-9

(continued)

TABLE III-7 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.5 ± 0.02		Inhalation chamber	Rats (pregnant)	~ 19 F	~ 19 F	4 h/d, for 19 d	19 d for 15 rats; others observed through delivery and growth of offspring	No overall toxic effects observed. Examination of females and fetuses at 20th d of pregnancy showed no deformities but slightly higher mortality of embryos. Development of offspring was normal except for a decrease in spontaneous mobility at one mo of age, which returned to near normal at 2 mo. Some changes in peripheral blood composition were reported at 2 mo.*	Sheveleva (1971) B-11
HCHO 0.4 ± 0.02		Inhalation chamber	Albino rats, 200-230 g (non-pregnant)	8-32 F	8-32 F	4 h/d	20 d	No effects on blood, urine, nervous system function, respiration, or weight.	Sanotskii et al. (1976) B-8
HCHO 0.4 ± 0.02		Inhalation chamber	Albino rats, 200-230 g (pregnant)	8-32 F	8-32 F	4 h/d	20 d	No effects on blood, urine, nervous system function, respiration, or weight.	Sanotskii et al. (1976) B-8
HCHO 0.2 + Phenol 0.5 + other resin decomposition products		80-85 g Phenol-HCHO resin was heated to 60°C. Static exposure in a 1-L chamber	Albino rats	5	5	2 h/d for 12 d	12 d	Behavior, threshold of excitability, and morphological composition of the blood showed no differences from those of the controls.	Galibin (1963) D-7

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* The Formaldehyde Panel (Griesemer et al., 1980) felt the no. of animals per dose level and no. of dose levels were inadequate and skeletal and soft tissue analyses were missing. Still, the Panel felt there were indications that HCHO affected reproductive potential.

(continued)

TABLE III-7 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.12 + 0.005 mg HCHO/L orally		Dynamic inhalation chambers	Rats	≥ 3 M	M; No. not given		Progeny studied up to 1 mo after birth	The exposed males showed a normal capacity to impregnate females with normal numbers of normal offspring.	Guseva (1972) B-6
HCHO 0.12		Hermetically sealed chambers	Random-bred rats	Not given	Not given	Daily for 3 mo	3 mo	Small regions of proliferation in the nasal mucosa with signs of protein dystrophy of the integumentary and glandular epithelia, pycnosis of the nuclei, desquamation, and deformation and agglutination of the ciliary borders. These and other changes in the nasal mucosa are reported as occurring whether the rats were exposed to HCHO or to benzene, toluene, xylene, m- and p-chlorophenyl isocyanate, chlorophos, hexane, and pentane at 10X their ambient air MAC's.	Bonashevskaya (1975) C-6
HCHO 0.1		Special 1 m^3 chambers	Albino rats, 130-240 g	50 M	50 M	90 d, continuous; 6-10 rats sacrificed every 30 d	90 d	DNA-ase activity of the liver increased and of the spleen decreased.	Tiunov and Ivanova (1976) B-8

(continued)

TABLE III-7 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.035		100-L chambers; 30 L air + HCHO per min	Albino rats	15 M	15 M	Continuous for 3 mo	3 mo	The structure of the amygdaloid complex was not different cytologically or neurologically from that of the controls. No change of chronaxy of the muscles-antagonists. No statistical change in cholinesterase activity.	Bonashevskaya (1973) B-8
HCHO 0.035 ± 0.004		Inhalation chamber, 100-L with air flow of 30 L/ min	Albino rats	25 M	25 M	Continuous	3 mo + 15-d recovery period	No effect on behavior or weight changes of animals. No effect on chronaxy of antagonistic muscles. No change in DNA or combined nucleic acids in cerebral hemispheres.	Fel'dman and Bonashevskaya (1971) B-10

(continued)

TABLE III-7 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.031 ± 0.002		100-L chambers; HCHO + air introduced at 30 L/min	Rats; avg. wt. of test rats, 179.0 ± 7.1 g; avg. wt. of controls, 162.0 ± 4.4 g	15-17 M	15-17 M	Continuous for 98 d except for days off and isolated working days	98 d + a recovery period whose length was not stated	No difference in behavior between test and control rats. Significant increase in weight gain compared to controls; 331.0 ± 12.5 g compared to 301.0 ± 6.0 g for the controls. However, the initial weight of the test group was also higher: 179.0 ± 7.1 vs. 162.0 ± 4.4 g. From ≧ 2 mo, the change in the summation of threshold indexes was significant (determined by electrical stimulation of a hind paw). With anodization of the brain as a functional stress, more distinct changes of the summation of threshold indexes occurred. Cholinesterase activity tended to decrease compared to that of the controls. No statistically significant effect on oxidase activity, SGOT, or erythrocyte and hemoglobin content of blood. The rhythm frequency of the heart action tended to increase and the electrical activity tended to decrease. There was also a decrease in the [heart] content of lipids and cholinesterase. The lungs showed weakly expressed fine foci of catarrh and foci of interstitial pneumonia; the liver, weakly expressed "hyperfunctional" regions of hepatocytes; brain cells, depletion of Nissl substance of the nerve cells having a disperse character in the cortex and especially in the Purkinje cells. These changes were preserved throughout the recovery period.	Dubrovskaya et al. (1976a) B-8

(continued)

TABLE III-7 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.012 ± 0.0015		100-L chambers; HCHO + air introduced at 30 L/min	Rats	15-17 M	15-17 M	Continuous for 98 d except for days off and isolated working days	98 d + an unspecified recovery period	No difference in behavior between test and control rats. Significant difference in the summation of threshold indexes at the end of the poisoning period (determined by electrical stimulation of a hind paw). Cholinesterase activity tended to decrease compared to that of the controls. As at 0.031 mg HCHO/m^3, there were changes in heart action--the rhythm frequency increased and the electrical activity decreased. No expressed pathological changes in the lungs, brain, and other organs except foci of catarrhal pneumonia and a focal (chiefly proliferative) process in the interalveolar septa, which decreased. Nerve cells recovered in the recovery period [one rat's brain cortex cells showed a lowering of Nissl substance].	Dubrovskaya et al. (1976a) B-8
HCHO 0.012		Hermetically sealed chambers	Random-bred rats	Not given	Not given	Daily for 3 mo	3 mo	Nasal mucosa was no different from that of the controls.	Bonashevskaya (1975) C-6
HCHO 0.012		100-L chambers; 30 L air + HCHO per min	Albino rats	15 M	15 M	Continuous for 3 mo	3 mo	The structure of the amygdaloid complex was not different cytologically or neurologically from that of the controls. No change in the chronaxy of the muscles-antagonists. No statistical change in cholinesterase activity.	Bonashevskaya (1973) B-8
HCHO 0.012 ± 0.002		Inhalation chamber; 100 L with air flow of 30 L/min	Albino rats	25 M	25 M	Continuous	3 mo + 15-d recovery period	No effect on behavior or weight changes of animals. No effect on chronaxy of antagonistic muscles.	Fel'dman and Bonashevskaya (1971) B-10

(continued)

TABLE III-7 (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.012		Inhalation chamber	Albino rats	10-12 F	10-12 F	Continuous 20 d; premating through pregnancy	~ 8 wk	Significant decrease in ascorbic acid in whole fetus, in female's liver, slight decrease in placenta; and significant increase in fetus' liver. Significant increase in nucleic acids in female's liver and significant decrease in DNA in female's and fetus' liver. Mean duration of pregnancy prolonged 14-15%. Avg. no. of fetuses 9.8 compared to 11.3 in controls. Significant decrease in fetal lung and liver weight and significant increase in weight of adrenals. No external deformities, no inhibitions of development of body systems, no macroscopic structural alterations in fetuses. Histochemical changes in fetuses included reduced glycogen content in the myocardium, accumulation of matter with a positive reaction to Schiff's reagent in the kidneys, and the presence of iron in Kupffer's cells.*	Pushkina and Gofmekler (1968) D-6 Gofmekler et al. (1968) D-6 Gofmekler (1968) D-5 Gofmekler and Bonashevskaya (1969) D-5

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* The Formaldehyde Panel (Griesemer et al., 1980) did not support the conclusions of Gofmekler et al. (1968) that HCHO significantly inhibited the synthesis of nucleic acid; they also point out the data do not support reported avg. no. of fetuses/litter; different articles give different nos. of females and fetuses.

TABLE III-8. RATS--CHRONIC EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 18.3 (14.6) HCl (10.6) Bis(chloromethyl) ether (0.001 estimated)			Rats, Sprague-Dawley	100 M	Presumably none	6 h/d, for 544 d	814 d 5 d/wk,	Squamous cell carcinomas of the nasal cavity developed in 25 rats; 2 developed benign papillomas of the nasal cavity. First deaths from cancer occurred at 305 d. Deaths occurred at 305-705 d from 1st exposure. The most common type of nasal cancer caused by bis(chloromethyl) ether (BCME), the reaction product of HCHO + HCl, is esthesioneuroepithelioma (tumor of the nerve tissue) and very seldom squamous cell carcinoma. This latter type of cancer had never been observed to occur spontaneously over many years of research with > 2,000 control animals, but it is the same type of tumor produced by approximately the same concentration of HCHO in the CIIT study with rats (Swenberg et al., 1980). In addition, no rat in this study developed lung cancer, but they did in BCME inhalation studies.	Nelson (1979) B-7 Selikoff and and Hammond (1981) C-- Griesemer et al. (1980) A--

(continued)

TABLE III-8 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 17.6 (14.1)	45 ± 5% 20-22°C	Hinners-type inhalation chamber; 12 air changes/h	Rats, Fisher 344, 7 wk	120 M 120 F	120 M 120 F	6 h/d, 5 d/wk	18 mo (of 24-mo study)	Dose-related decrease in body weight and yellow discoloration of haircoat. Forty-four deaths of which 1 had osteomalacia; 1, epithelial dysplasia; 38, squamous metaplasia; 11, squamous or epithelial hyperplasia; 6, squamous papillary hyperplasia; 3, squamous metaplasia with cellular atypia; 4, squamous papilloma; 28, squamous cell carcinoma; and 1, spindle cell sarcoma. Forty animals were sacrificed and nasal turbinates examined; 2 had focal turbinate atrophy; 13, epithelial dysplasia; 39, squamous metaplasia; 15, squamous or epithelial hyperplasia; 4, squamous papillary hyperplasia; 7, squamous metaplasia with cellular atypia; 1, adenomatous polyp; and 8, squamous cell carcinoma. Most of the animals examined had rhinitis, acute suppurative or seropurulent. Most of the lesions were dose-related with respect both to severity and extent of involvement. Sharp increase in deaths after 12 mo. No abnormalities in other tissues or control animals. Initiating and/or promoting activities of sialodacryoadenitis virus cannot be ruled out. Mice exposed to this concentration did not develop nasal cavity tumors. Selikoff and Hammond (1981) concluded after they had examined the 24-mo results (a total of 95 nasal cavity carcinomas had developed) that the "HCHO exposure and not the viral infec- appears to be the crucial factor in development of nasal carcinomas" in this study.	Swenberg et al. (1980) B-15

(continued)

TABLE III-8 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 7.0 (5.6)	45 ± 5% 20-22°C	Hinners-type inhalation chamber; 12 air changes/h	Rats, Fischer 344, 7 wk	120 M 120F	120 M 120F	6 h/d, 5 d/wk	18 mo (of 24-mo study)	Dose-related decrease in body weight and yellow discoloration of haircoat. Eight deaths, of which all had epithelial dysplasia and 6 squamous metaplasia of the nasal turbinates. Forty animals were sacrificed and nasal turbinates examined; 37 had epithelial dysplasia, 35 had squamous metaplasia, and 1 had adenomatous polyp. Seven of the 40 had rhinitis, acute suppurative or seropurulent. No abnormalities in other tissues or in controls. By 16 mo, one rat developed a squamous cell carcinoma of the facial skin that did not extend into the turbinate. At 24 mo, 2 rats had developed squamous cell carcinomas of the nasal turbinates.	Swenberg et al. (1980) B-15 NIOSH/OSHA (1980) C--
HCHO 3.75 (3)		Inhalation	Rats	20 M 20 F	20 M 20 F	22 h/d 7 d/wk 6 mo	6 mo	Decreased rate of body weight gain.	Clary (1980) B--
HCHO ~ 2.6 (2.1)	45 ± 5% 20-22°C	Hinners-type inhalation chamber; 12 air changes/h	Rats, Fischer 344, 7 wk	120 M 120 F	120 M 120 F	6 h/d, 5 d/wk	18 mo (of 24-mo study)	Dose-related decrease in body weight and yellow discoloration of haircoat. Two deaths, of which one had epithelial dysplasia of the nasal turbinates. Forty animals were sacrificed and nasal turbinates examined; 35 had epithelial dysplasia and 24 had squamous metaplasia. Two of the 40 had rhinitis, acute suppurative or seropurulent. No abnormalities in other tissues or in controls.	Swenberg et al. (1980) B-15
HCHO 1.25 (1)		Inhalation	Rats	20 M 20 F	20 M 20 F	22 h/d 7 d/wk 6 mo	6 mo	No adverse effects noted while exposed or on pathological evaluation.	Clary (1980) B--

(Continued)

TABLE III-8 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 1.0		150-L inhalation chamber with air flow of 30 L/min	Albino rats, Wistar, 130-150 g Pregnant during 8th mo.	8 F	8 F	Continuous, 8 mo	8 mo	Body wt. increased during exposure, no significant differerence in blood cholinesterase activity, erythrocyte count, and hemoglobin level or in the activity of asparagine aminotransferase in the blood plasma.	Misiakiewicz et al. (1977) C-7
HCHO 1.0		150-L inhalation chamber with air flow of 30 L/min	Rats, offspring of mothers exposed to 1 mg HCHO/m^3 for 8 mo including duration of pregnancy	Nos. not given	Nos. not given, Group I offspring of exposed mothers, Group II, offspring of unexposed mothers	Continuous, 8 mo	8 mo	Exposed rats had a 10% smaller increase in body wt.; controls in Group I had a 7.5% smaller increase than controls in Group II. Between the 3 groups, no significant differences in blood cholinesterase activity, erythrocyte count, and hemoglobin level or in the activity of asparagine aminotransferase in the blood plasma. No significant differences in wt. coefficients of kidneys, spleen, or liver of 3 groups except for a significant decrease in wt. coefficient of liver of exposed rats compared to control Group II. Morphological changes in upper respiratory tract in control Group I. Same changes but more numerous in exposed rats compared to completely unexposed control Group II.	Misiakiewicz et al. (1977) C-7
HCHO 0.5-0.6 MeOH 5.0-6.0 following intratracheal introduction of resin-treated or untreated coal dust			Rats	Not given	No. not given. Rats dosed with untreated coal dust and not exposed to HCHO and MeOH	6 mo, continuous ?	6 mo	The collagen content per identical lung weight was significantly higher in the exposed group that had been dosed with untreated coal dust. More severe disturbances in lung structure both in the bronchial tree and the respiratory branch occurred in exposed rats pre-dosed with treated dust. The changes in the bronchi were also more severe in the exposed rats than in the controls.	Gadzhiev et al. (1977) D-4

(continued)

TABLE III-8 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.5 + 0.1 HCHO/L orally		Inhalation chambers	Rats	20 M	20 M	4 h/d, 5X/wk for 7 mo (oral doses introduced through a probe in the same period)	7 mo	2 mo--Disturbance in conditioned reflex shown by lowering of latent period toward light. Tendency to increased alanine aminotransferase and cholinesterase activities and the amount of protein in the blood serum. 3 mo--Change in biochemical indexes of the blood. Increases in content of histamine and SH groups, decrease in the activity of alanine aminotransferase, and a tendency toward lowering oxidase activity. 4-6 mo--Normalization of all earlier appearing shifts 5 mo--Tests using hexobarbital, alcohol, or brain anodization as stresses showed inhibition of conditioned reflex activity and the brain cortex. 7 mo--Increase of histamine in blood. Mummification of cellular elements in the epithelium of the respiratory tract and upper portions of the alimentary tract. Activities of cholinesterase and alanine aminotransferase in the liver increased but cholinesterase decreased in brain tissue. The increase in Vitamin C in the adrenals indicated disturbance of compensating mechanisms. Degenerative changes were found in the olfactory, optic, and auditory analyzers.	Guseva (1973) C-8

(continued)

TABLE III-8 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.5 + 0.1 mg HCHO/L orally		Dynamic inhalation chambers	Rats	$\geq$ 3 M	M; No. not given	4 h, 5X/wk for 6 mo (Oral doses given at same time)	6 mo + progeny studied up to 1 mo after birth	The ability of the exposed males to impregnate untreated females (2 per test male) was not affected. The number and weight of the fetuses and newborn rats fathered by the treated males did not differ significantly from those of the control group. Defects and anomalies were not found in the offspring nor did any significant differences develop in the offspring in their first month after birth. Pituitary preparation from the exposed rats did not cause any differences in gonadotropic reaction when injected into immature females. A significant decrease was observed in the amount of nucleic acids in the males' testicles, which was attributed to gonadotropic poisoning by HCHO.	Guseva (1972) B-6

(continued)

TABLE III-8 (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.5		Inhalation chamber	Albino rats, 180-240 g	60 M	60 M	5h/d, 6 d/wk	6 mo + 1-mo recovery	General health good, behavior normal, and body weight increased steadily. No substantial change in the structure of the upper respiratory tract, lungs, or other internal organs. Minor changes in blood and urine parameters reported. During the 2nd mo, the eosinophil count increased significantly as did the daily phenol red excretion in the urine. Urinary hippuric acid secretion dropped significantly. At end of study, the weight coefficient of the testicles had decreased significantly. At 1 mo post-exposure, only the phenol red excretion in the urine was still significantly higher; all other factors had returned to normal (weight coefficients not determined).	Nagornyi et al. (1979) B-9
HCHO 0.5		200-L inhalation chambers	Rats	25 F	25 F	4 h/d for 4 mo	4 mo	Within 2-3.4 mo, exposure to HCHO (and in a separate experiment to the same level of phenol) increased the activities of cholinesterase, oxidase, and glutaminoaspartic aminotransferase and lowered the nucleic acid and total protein content of the serum. The SGOT in liver homogenates was increased, but the activities of cholinesterase and aspartic transferase were decreased.	Pod''yacheva (1977) C-9

(continued)

TABLE III-8 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.25 + 0.01 mg HCHO/L orally		Inhalation chambers	Rats	20 M	20 M	4 h/d 5X/wk for 7 mo	7 mo	No reliable difference in the indexes of the conditioned reflex from those of the control group during the whole study.	Guseva (1973) C-8
						(Oral doses through a probe in the same period.)		$\leq$ 3 mo--Change of biochemical indexes of blood characterized chiefly by a tendency to an increase in cholinesterase activity, histamine content, and number of SH groups.	
								4-6 mo--All indexes studied within physiological norms.	
								5 mo--Tests using hexobarbital, alcohol, brain anodization as stresses showed inhibition of conditioned reflex activity and the brain cortex.	
								7 mo--Slight increase in histamine content and amount of protein in blood serum.	
HCHO 0.25 + 0.01 mg HCHO/L orally		Dynamic inhalation chambers	Rats	$\geq$ 3 M; No. not given	M; No. not given	4 h 5X/wk for 6 mo (oral doses given at same time)	6 mo	A significant decrease was observed in the amount of nucleic acids in the males' testicles, which was attributed to gonadotropic poisoning by HCHO.	Guseva (1972) B-6
HCHO 0.25 Phenol 0.25		200-L inhalation chambers	Rats	25 F	25 F	4 h/d for 4 mo	4 mo	The effects at 0.5 mg HCHO or phenol per cubic meter air were duplicated when the two were combined at 0.25 mg/m^3 each. However, the changes occurred sooner--at 0.5-1 mo compared to 2-3.4 mo.	Pod"yacheva (1977) C-9

(continued)

TABLE III-8 (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)		Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO	0.25 (0.2)		Inhalation	Rats	20 M 20 F	20 M 20 F	22 h/d 7 d/wk 6 mo	6 mo	No adverse effects noted while exposed or on pathological evaluation.	Clary (1980) B--
HCHO	0.12 + 0.005 mg HCHO/L orally		Inhalation chambers	Rats	20 M	20 M	4 h/d 5X/wk for 7 mo (oral doses given in same period)	7 mo	No significant differences in the conditioned reflex action or of the biochemical indexes of the blood during the whole experiment. No significant differences in cholinesterase activity, alanine and asparagine aminotransferase activities, and histamine content in the liver; cholinesterase in the brain; or vitamin C in the adrenals. No abnormalities found in pathomorphological and neurohistological studies. Little or no change in CNS activity from that of controls upon stressing with alcohol or brain anodization in the 5th mo.	Guseva (1973) C-8

(Continued)

TABLE III-8 (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.035		100-L inhalation chamber	Rats, Wistar, 180 ± 10 g	30 M	30 M	3 h/d, 60 mo	6 mo	No observed changes in behavior, general condition, and wt. of rats. Significant decrease of 20-30% or more in the bioenergetic metabolism processes in the mitochondrial fraction of liver. Processes with such decreases were: activity of cytochrome oxidase, and succinic dehydrogenase; respiration; O_2 consumption; CO_2 elimination; esterification of inorganic phosphorus; and rate of oxidative phosphorylation. Slight increase in lactic acid content of blood. Significant increase of pyruvic acid in blood and hemoglobin content in serum. All the above changes were noted in mo 1 and continued through mo 6.	Basmadzhieva et al. (1974) B-9
HCHO 0.035			Albino rats, Wistar, 180 ± 10 g	20 M	20 M	8 h/d, 6 mo	6 mo	No observed changes in behavior and general condition of animals. After 2 and 6 mo, a significant decrease in RNA content in testicular homogenate; however, at 4 mo, it was increased. DNA content in testicular homogenate increased and remained increased over 6 mo, but deoxyribonuclease activity was significantly decreased. Decrease in soluble protein content in testicular homogenate corresponding with changes in RNA content. Decrease in spermatozoon mobility.	Davidkova and Basmadzhieva (1979) B-7

TABLE III-9. GUINEA PIGS--ACUTE EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 63 (50)		Dynamic inhalation chamber	Guinea Pigs	3	Served as own control	4 h, once	6.5 h	Lung resistance more than tripled in first h to its highest level during the exposure but had not returned to normal 2 h post-exposure.	Amdur (1960) B-13
HCHO ~ 63 ± 10 (50±8)		Dynamic inhalation chamber	Guinea Pigs breathing through cannula in trachea	6	Served as own control	1 h, once	2.5 h	Significant increase in lung resistance and in work required to breathe and significant decrease in lung compliance, breathing frequency, and minute volume. At 1 h post-exposure, lung resistance was still significantly higher than pre-exposure.	Amdur (1960) B-13
HCHO ~ 62.5 (50)		Inhalation chamber, exposed head only	Guinea Pigs	Not given	Not given	1 h, once	1 h	Significant increase in resistance and tidal volume and significant decrease in respiratory rate and minute volume of lungs. No change in lung compliance.	Davis et al. (1965) C-5 Davis et al. (1967) D-6
HCHO ~ 62.5 (50)		Inhalation chamber, exposed head only	Guinea Pigs breathing through tracheotomy	Not given	Not given	1 h, once	1 h	No change in lung compliance, resistance, tidal volume, minute volume, or respiratory rate.	Davis et al. (1965) C-5 Davis et al. (1967) D-6
HCHO ~ 61 ± 11 (49 ± 9)		Dynamic inhalation chamber	Guinea Pigs	11	Served as own control	1 h, once	2.5 h	Highly significant increase in lung resistance and decrease in lung compliance and breathing frequency. Significant increase in work required to breathe and in lung tidal volume, slightly significant decrease in lung minute volume. At 1 h post-exposure, lung resistance was still significantly higher than pre-exposure.	Amdur (1960) B-13

(continued)

TABLE III-9 (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 59 ± 16 (47 ± 13) NaCl 10.0 ± 1.9		Dynamic inhalation chamber	Guinea Pigs	8	Served as own control	1 h, once	2.5 h	Highly significant increase in lung resistance. Significant decrease in compliance, breathing frequency, and minute volume and increase in tidal volume and work required to breathe. At 1 h post-exposure, lung resistance was still significantly increased over pre-exposure.	Amdur (1960) B-13
HCHO ~ 34 ± 8 (27 ± 6) NaCl 12.1 ± 2.1		Dynamic inhalation chamber	Guinea Pigs	12	Served as own control	1 h, once	2.5 h	Highly significant increase in lung resistance. Significant decrease in compliance and breathing frequency and increase in tidal volume and work required to breathe. At 1 h post-exposure, lung resistance was still significantly increased over pre-exposure.	Amdur (1960) B-13
HCHO ~ 25 ± 4.8 (20 ± 3.8)		Dynamic inhalation chamber. Breathing through cannula in trachea	Guinea Pigs	10	Served as own control	1 h, once	2.5 h	Highly significant increase in lung resistance and decrease of compliance. Significant decrease in breathing frequency and lung minute volume. Insignificant increase in work required to breathe. At 1 h post-exposure, lung resistance was still slightly but insignificantly increased over pre-exposure.	Amdur (1960) B-13
HCHO ~ 15.6 (12.5)		Nose mask	Guinea Pigs	9	Served as own control	1.5 h, once	1.5 h,	Significant increase in respiratory rate, flow resistance, and tidal volume compared to pre-exposure values.	Murphy and Ulrich (1964) D-5

(continued)

TABLE III-9 (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 13.8 ± 3.6 (11.0 ± 2.9)		Dynamic inhalation chamber	Guinea Pigs	10	Served as own control	1 h, once	2.5 h	Significant increase in lung resistance, highly significant decrease in lung compliance. Slight but insignificant increase in work required to breathe. Significant decrease in breathing frequency and minute volume of lungs. At 1 h post-exposure, lung resistance still slightly but insignificantly increased over pre-exposure.	Amdur (1960) B-13
HCHO ~ 13.5 ± 0.6 (10.8 ± 0.5) NaCl 10.7 ± 1.7		Dynamic inhalation chamber	Guinea Pigs	8	Served as own control	1 h, once	2.5 h	Highly significant increase in lung resistance and decrease in lung minute volume. Significant decrease in compliance and slightly significant increase in work required to breathe. At 1 h post-exposure, lung resistance was still significantly increased over pre-exposure.	Amdur (1960) B-13
HCHO ~ 6.5 ± 0.08 (5.2 ± 0.07)		Dynamic inhalation chamber. Breathing through cannula in trachea	Guinea Pigs	7	Served as own control	1 h, once	2.5 h	Significant increase in lung resistance; significant decrease in compliance, breathing frequency, and lung minute volume. Slight insignificant increase in work required to breathe and in lung resistance 1 h post-exposure compared to pre-exposure.	Amdur (1960) B-13
HCHO ~ 4.9 (3.9)		Nose mask	Guinea Pigs	10	Served as own control	1.5 h, once	1.5 h	Significant increase in respiratory rate, flow resistance, and tidal volume compared to pre-exposure values.	Murphy and Ulrich (1964) D-5

(continued)

TABLE III-9 (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 4.5 ± 0.6 (3.6 ± 0.5) NaCl 10		Dynamic inhalation chamber. Breathing through cannula in trachea	Guinea Pigs	6	Served as own control	1 h, once	2.5 h	Significant increase in lung resistance and decrease in compliance, breathing frequency, and minute volume. Slight but insignificant increase in work required to breathe. At 1 h post-exposure, lung resistance was still significantly higher than pre-exposure.	Amdur (1960) B-13
HCHO ~ 4.5 ± 0.4 (3.6 ± 0.3)		Dynamic inhalation chamber	Guinea Pigs	10	Served as own control	1 h, once	2.5 h	Highly significant increase in lung resistance, significant increase in work required to breathe. Slightly significant decrease in lung compliance. At 1 h post-exposure, lung resistance still slightly but insignificantly increased over pre-exposure.	Amdur (1960) B-13
HCHO ~ 3.3 ± 0.4 (2.6 ± 0.3) NaCl 8.7 ± 0.9		Dynamic inhalation chamber	Guinea Pigs	8	Served as own control	1 h, once	2.5 h	Highly significant increase in lung resistance. Significant decrease in compliance and increase in work required to breathe. At 1 h post-exposure, lung resistance was still significantly increased over pre-exposure.	Amdur (1960) B-13
HCHO ~ 1.52 ± 0.29 (1.22 ± 0.23)		Dynamic inhalation chamber	Guinea Pigs	4	Served as own control	1 h, once	2.5 h	Significant increase in lung resistance and in work required to breathe. Slight decrease in lung compliance and breathing frequency. At 1 h post-exposure, lung resistance still slightly but insignificantly increased over pre-exposure.	Amdur (1960) B-13

(continued)

TABLE III-9 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 1.43 ± 0.1 NaCl 10		Dynamic inhalation chamber. Breathing through cannula in trachea	Guinea Pigs	8	Served as own control	1 h, once	2.5 h	Significant increase in lung resistance and in work required to breathe. Significant decrease in lung compliance. At 1 h post-exposure, lung resistance was still significantly higher than pre-exposure.	Amdur (1960) B-13
HCHO ~ 1.13 ± 0.1 (0.90 ± 0.08)		Dynamic inhalation chamber. Breathing through cannula in trachea	Guinea Pigs	7	Served as own control	1 h, once	2.5 h	Highly significant increase in lung resistance and decrease in compliance and insignificant increase in work required to breathe. At 1 h post-exposure, lung resistance was still slightly but insignificantly increased over pre-exposure.	Amdur (1960) B-13
HCHO ~ 0.96 ± 0.34 (0.76 ± 0.27) NaCl 12.8 ± 2.0		Dynamic inhalation chamber	Guinea Pigs	8	Served as own control	1 h, once	2.5 h	Highly significant increase in lung resistance and significant decrease in compliance. Slightly significant increase in work required to breathe. At 1 h post-exposure, lung resistance was still significantly increased over pre-exposure.	Amdur (1960) B-13
HCHO ~ 0.73 ± 0.1 (0.58 ± 0.08)		Dynamic inhalation chamber	Guinea Pigs	23	Served as own control	1 h, once	2.5 h	Highly significant increase in lung resistance and decrease in compliance. Insignificant increase in work required to breathe. At 1 h post-exposure, lung resistance still slightly but insignificantly increased over pre-exposure.	Amdur (1960) B-13
HCHO ~ 0.4 ± 0.03 (0.32 ± 0.02) NaCl 11.3 ± 1.6		Dynamic inhalation chamber	Guinea Pigs	8	Served as own control	1 h, once	2.5 h	Significant increase in lung resistance and decrease in compliance. Slightly significant increase in work required to breathe. At 1 h post-exposure, lung resistance was still significantly increased over pre-exposure.	Amdur (1960) B-13

(continued)

TABLE III-9 (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 0.39 ± 0.1 (0.31 ± 0.08)		Dynamic inhalation chamber	Guinea Pigs	13	Served as own control	1 h, once	2.5 h	Significant increase in lung resistance and decrease in lung compliance. Insignificant increase in work required to breathe. At 1 h post-exposure, lung resistance near normal.	Amdur (1960) B-13
HCHO ~ 0.09 ± 0.01 NaCl 7.5 ± 0.7		Dynamic inhalation chamber	Guinea Pigs	4	Served as own control	1 h, once	2.5 h	Significant increase in lung resistance. Insignificant decrease in compliance and increase in work required to breathe. At 1 h post-exposure, lung resistance was still slightly but insignificantly increased over pre-exposure.	Amdur (1960) B-13
HCHO ~ 0.06 ± 0.03 (0.05 ± 0.02)		Dynamic inhalation chamber	Guinea Pigs	18	Served as own control	1 h, once	2.5 h	Slight but insignificant increase in lung resistance and work required to breathe, slight decrease in lung compliance. At 1 h post-exposure, lung resistance still slightly but insignificantly increased over pre-exposure.	Amdur (1960) B-13

TABLE III-10. GUINEA PIGS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 15			Guinea Pigs, light colored	M No. not given	M No. not given	Continuous	39 h + 1 mo	Time until cholinesterase activity was lowered by 25-30% compared to that of the controls--39 h. Time until leukocyte number was increased by 25-30% compared to that of controls--39 h. Allergic effects were not observed.	Ostapovich (1975) C-6
HCHO ~ 12.5 (10)		Not given	Guinea Pigs	Not given	Not given	4 h/d, 5 d/wk	13 wk + 3 d	Lung glutathione significantly higher compared to controls. Liver and kidney glutathione levels were lower but not significantly different. Glutathione reductase activities of lung, liver, and kidney were lower; liver and kidney decreases were significant.	Mecler (1978) D-4
HCHO 7			Guinea Pigs, light colored	M		Continuous	168 h (7 d) + 1 mo	Time until cholinesterase activity was lowered by 25-30% compared to that of the controls--120 h. Time until leukocyte number was increased by 25-30% compared to that of the controls--144 h. Time until allergic effects--168 h. Thus, toxic effects appeared somewhat sooner than allergic effects.	Ostapovich (1975) C-6

(continued)

TABLE III-10 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 7; avg. concentration 2.3 due to intermittency of exposure			Guinea Pigs, light colored	M No. not given	M No. not given	8 h/d	≤704 h (29.3 d) + 1 mo	Time until cholinesterase activity was 25-30% less than that of the controls--608 h (exposure time 208 h), much longer than during continuous exposure. Time until leukocyte number was 25-30% higher than that of the controls--704 h (exposure time 240 h). Time until allergic effects--168 h (exposure time 56 h), the same as during continuous exposure to 7 mg HCHO/m^3. Thus, allergic effects appeared sooner than toxic effects.	Ostapovich (1975) C-6
HCHO 7; avg. concentration 3.5 due to intermittency of exposure			Guinea Pigs, light colored	M No. not given	M No. not given	Exposed for 24 h every other day	≤ 504 h (21 d) + 1 mo	Time until cholinesterase activity was 25-30% less than that of the controls--432 h (exposure time 216 h). Time leukocyte number was 25-30% higher than that of the controls--504 h (exposure time 264 h). Allergic effects were not observed. Thus, only toxic effects appeared.	Ostapovich (1975) C-6
HCHO 4.6±0.4	50% 77 ± 2°F	Inhalation chamber (modified Rochester-type) Airflow 1.2 m^3/min	Guinea Pigs, Princeton-derived	15 M&F	No. not given	Continuous for 90 d (< 2.2% down time)	90 d	No deaths. Hematologic values were normal. Lungs showed varying degrees of interstitial inflammation and heart and kidneys showed focal chronic inflammatory changes.	Coon et al. (1970) B-12

(continued)

TABLE III-10 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 2			Guinea Pigs, light colored	M No. not given	M No. not given	Continuous	1,272 h (53 d) + 1 mo	Time until cholinesterase activity was 25-30% less than that of the controls--1,272 h. Time until leukocyte number was 25-30% higher than that of the controls--936 h. Time until allergic effects--336 h. Thus, allergic effects appeared much sooner than toxic effects.	Ostapovich (1975) C-6
HCHO 0.5		Inhalation chamber	Guinea Pigs	15	15	5 h/d, 6 d/wk	1 mo	General health good and body weight increased steadily. No substantial change in the structure of the upper respiratory tract, lungs, or other internal organs. Minor changes in blood and urine parameters reported.	Nagornyi et al. (1979) B-9
HCHO 0.38 (Level chosen because it is similar to a typical main highway concentration)		Not given	Guinea Pigs	M & F No. not given	M & F No. not given	8 h/d for 21 d	5 wk	Injury of the neutrophils. Degranulation of basophilic cells after the 21-d period of sensitization and 2 wk after was less than that seen when the guinea pigs were exposed to 0.038 and 0.011 mg HCHO/m^3. Others have also noted that chemical allergens give the most expressed sensitizing effect at the lowest concentrations. Formation of antibodies occurred.	Vinogradov et al. (1974) B-7

(continued)

TABLE III-10 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.038		Not given	Guinea Pigs	M & F No. not given	M & F No. not given	8 h/d for 21 d	5 wk	Injury of the neutrophils not so extensive as at 0.38 and 0.011 mg HCHO/m^3. Degranulation of basophils less than at 0.011 mg/m^3 and more than at 0.38 mg/m^3 after the 21 d sensitization period but was highest 2 wk later. A higher titer of antibodies in bound complement was found at both times than when the guinea pigs had been exposed to 0.011 or 0.38 mg HCHO/m^3.	Vinogradov et al. (1974) B-7

(continued)

TABLE III-10 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.011		Special inhalation chambers	Guinea Pigs, avg. wt. 200-250 g	~ 16	~ 16	7 h/d for 30 d	> 3 mo	Four weeks of poisoning by HCHO caused an active phagocytic reaction related mostly to the digestive function of the cells. The phagocytic ability of the neutrophils was greatest 4 wk after the end of poisoning. Within 2 mo after poisoning, all the increased indexes of absorptive and digestive functions seen at 4 wk after were normal. An especially high titer of serum complement was noted within 2 wk after the end of poisoning. The basic indexes of the white blood were little changed and were within the norms during or after poisoning. After 2 mo of observation after the poisoning, the animals were subjected to stress in the form of hypoxia. The test animals showed a lowering of the content of most of the cellular elements after hypoxia while the controls generally showed increases. The immune response of previously poisoned animals was significantly depressed compared to controls after hypoxia. In the controls, hypoxia caused a decrease in phagocytic number and index but did not change the digestion process appreciably. In the test animals, hypoxia depressed the indexes of phagocytosis, especially the digestive capacity of the neutrophils. Hypoxia led to an insignificant lowering of the titer of serum complement in the controls, whereas the test animals showed a significant lowering of complement activity.	Vinogradov and Rudnev (1976) B-7

(continued)

TABLE III-10 (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.011		Not given	Guinea Pigs	M & F No. not given	M & F No. not given	8 h/d for 21 d	5 wk	Injury of the neutrophils. Degranulation of basophils was highest at this level after 21 d of sensitization. Others have also noted that chemical allergens give the most expressed sensitizing effect at the lowest concentrations. Formation of antibodies occurred.	Vinogradov et al. (1974) B-7

TABLE III-11. RABBITS--ACUTE EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 3.5-6.5			Rabbits	≤ 47	Not given	10 s once	15-20 s	Threshold of individual sensitivity for an adaptive olfactory reaction. Fast recovery to original state.	Bokina and Eksler (1973) B-7
HCHO ~ 6 (5)		Head only, with exposure mask, air flow 4 L/min	Rabbit 2.8-3.4 kg	2-5 M		3-4 min		Decrease in blood pressure, marked decrease in heart rate and respiratory movement.	Ikeda et al. (1980) C-7
HCHO 2-3.5			Rabbits	≤ 47	Not given	10 min		Disturbance in the long-term (3-5 min) synchronized rhythm and breathing disorganization. Changes in the functional condition of the rabbits were characterized by prolonged periods of theta-rhythm in the electrical activity of the brain. The reaction was early, generalized, and more distinct with HCHO than with O_3. The effect of HCHO may be its effect on the trigeminal nerve and the connection of this nerve with the reticular formation, which in its turn diffusely activates the whole brain.	Bokina and Eksler (1973) B-7

(continued)

TABLE III-11 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 2-3.5			Rabbits	$\leq$ 47	Not given	10 s once	15-20 s	Threshold of individual sensitivity for the orientation-exploratory reaction, i.e., the Pavlovian reflex that ensures a response from the CNS to constantly changing conditions. Fast recovery to original state. The nonspecific reaction of orientation and exploration is characterized by the appearance in the neocortex of individual flashes of activity and by quickened respiration. Olfactory analyzer structures show no change in EEG activity. The form of the EEG response to concentrations of chemical substances eliciting the orienting-exploratory reaction coincides with that to light and sound. Thus, the CNS evaluates these sensory stimuli as undifferentiated (Bokina et al., 1976).	Bokina and Eksler (1973) B-7

(continued)

TABLE III-11 (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.65 + binocular light stimulation: A series of light flashes comprising 10 impulses with frequencies of 4 and 7 Hz, both of which were tested 5 times in a given segment of the test with 15-20 s between the separate series.		Constant stream of HCHO-air mixture (pure air for the controls) supplied at a rate of 8 L/min, which produced an insignificant tactile action. Light source was a gas-discharge lamp at 20 cm from the head of constrained rabbit. The series of flashes of both frequencies were imposed 4 times: in the background period, at the 10th and 20th min of exposure, and within 10 min after exposure ended.	Rabbits 2.5 kg	5 M	5 M	20 min	30 min	Reactions of rearrangement [synchronization] of rhythm were observed by EEG for all studied brain structures. At the 20th min, statistically significant deterioration of the reaction of rearrangement of rhythm arose in the corticomedial nucleus of the amygdala. The shift did not disappear within 10 min after cessation of the exposure. There was also a change in the overall EEG, wherein persistent stress dominated the rhythm.* Analogous deterioration of the reactions of rearrangement of rhythm in rabbits at low light frequencies upon exposure to narcotics was reported by A. A. Razumeev. Fel'dman and Eksler (1975) proposed that the effects seen in their test also reflect the early nontoxic but incipient narcotic and therefore unfavorable action of HCHO.	Fel'dman and Eksler (1975) B-7 Bokina and Eksler (1973) B-7

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* The persistent stress rhythm that develops in the cortex and limbic reticular structures correlates in some animals with an avoidance reaction. Such a protracted generalized stress rhythm indicates an adverse response of the CNS to the odorous substance (Bokina et al., 1976).

(continued)

TABLE III-11 (concluded)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.035 + binocular light stimulation: A series of light flashes comprising 10 impulses with frequencies of 4 and 7 Hz, both of which were tested 5 times in a given segment of the test with 15-20 s between the separate series.		See previous entry	Rabbits 2.5 kg	5 M	5 M	20 min	30 min	No effect on the reaction of the rearrangement of rhythm or on the overall electrical activity of the brain.	Fel'dman and Eksler (1975) B-7 Bokina and Eksler (1973) B-7

TABLE III-12. RABBITS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 3.7-6.5 + Noise			Rabbits	≤ 47	Not given	Not given	"Short term"	Habituation to the irritant occurred. HCHO changed the total functional condition of the brain (activation). The high sensory input into the olfactory structures, the authors proposed, leads to development of paroxysmal activity in the olfactory analyzer structures.	Bokina and Eksler (1973) B-7
HCHO 4.6 ± 0.4	50% 77 ± 2°F	Inhalation chamber (modified Rochester-type) Airflow 1.2 m^3/min.	Rabbits, New Zealand albino	3 M	No. not given	Continuous for 90 d	90 d	No deaths. Hematologic values were normal. Lungs showed varying degrees of interstitial inflammation.	Coon et al. (1970) B-12
HCHO 2-3.7			Rabbits	≤ 47	Not given	Intermittent exposure; time not specified		Slight drowsiness as evidenced by EEG.	Bokina and Eksler (1973) B-7
HCHO 0.65 + stress by rhythmic light			Rabbits	≤ 47	2-4 wk			Provocation in the olfactory bulb and corticomedial amygdala of latent hidden foci of paroxysmal activity. Thus, the specific structures of the olfactory analyzer are the initial responders to the pathological actions of odorous substances.	Bokina and Eksler (1973) B-7

(continued)

TABLE III-12 (concluded)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.1 + functional stress by pentylenetetrazole			Rabbits	≤ 47	Not given	1.5 mo		Evoked potentials of the visual cortex were studied. A variety of minor changes were found, but there were no nonequivocal pathologic effects.	Bokina and Eksler (1973) B-7

TABLE III-13. CATS--ACUTE EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 9,630		Inhalation chamber	Cat, 3.2 kg	1	None	3.3 h	3.3 h	Immediate sneezing, tearing, saliva secretion, mouth breathing, and dyspnea. Vomiting movements later; at 1.5 h, cat lying down; after 2 h, unable to stand up. Respiration continued very irregularly along with body spasms until death at 200 min. Autopsy found blood in nose, larynx damaged, tracheal mucosa loosened, heart damaged, eyes bloody.	Iwanoff (1911) C-8
HCHO 6,330		Inhalation chamber	Cat, 2 kg	1	None	3 h, once	3.3 h	Immediate restlessness, saliva secretion, eyes closed, respiration 28. Later respiration decreased, dyspnea. After 2 h, vomiting of white foamy liquid. Death 20 min after exposure ends. Autopsy finds normal eyes, mouth, nose, heart, and kidneys. Slight hyperemia of brain, coagulated fibrinous liquid in trachea, and 1/3 of lung functioning hindered by hyperemia, edema, and bleeding.	Iwanoff (1911) C-8

(continued)

TABLE III-13 (concluded)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 2,010		Inhalation chamber	Cat, 2.0 kg	1	None	4.6 h, once	4 d	Immediate and distinct effects: tearing, sneezing, coughing, irregular breathing. Later, dyspnea and mouth breathing, vomiting of white foamy liquid. At end of exposure, severe dyspnea and death on 4th d.	Iwanoff (1911) C-8
HCHO 825		Inhalation chamber	Cat, 2.6 kg	1	None	8 h, once	4 d	Irregular respiration, dyspnea, coughing, body trembling, vomiting movements. At end of exposure, cat breathing with difficulty, condition worsened, death on 4th d.	Iwanoff (1911) C-8
HCHO 820		Inhalation chamber	Cat, 2.7 kg	1	None	8.6 h, once	6 d	Respiration increased, sneezing, coughing, difficulty in breathing, increased saliva secretion. No recovery after exposure; cat died on 6th d.	Iwanoff (1911) C-8
HCHO 820		Inhalation chamber	Cat, 1.8 kg	1	None	4 h, once	Observed for several days after exposure	Coughing, respiration 16, increased saliva secretion, condition worsened during exposure. Cat recovered after several days.	Iwanoff (1911) C-8
HCHO 260		Inhalation chamber	Cat, 3 kg	1	None	3.5 h, once	Observed for several days after exposure	Respiration slowed, sneezing, coughing, increased saliva and tear secretion, eyes kept closed after 2 h, slight dyspnea. Cat recovered after exposure.	Iwanoff (1911) C-8

TABLE III-14. PIGS--ACUTE EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO ~ 2.5 (2.0)		Anesthetized, with artificial ventilation	Pigs, 21.7 ± 1.4 kg, 6-8 wk	8	None	6 h, once	6 h	No significant change in lung compliance values or blood gas values. Moderate morphologic changes in lungs, desquamation of alveolar cover cells, some intra-alveolar and interstitial edema, emphysema, and atelectasis. These changes more evident in dorsal lung section than in the ventral section. Similar effects occurred in "control" pigs exposed to ~ 0.03 mg/m^3.	Frey et al. (1979) B-12
HCHO ~ 0.25 (0.2)		Anesthetized, with artificial ventilation	Pigs, 21.7 ± 1.4 kg, 6-8 wk	7	None	6 h, once	6 h	Significant decrease in lung compliance values from beginning of study to end. Blood gas values fluctuated but did not change significantly. Slight interstitial edema, emphysema, and atelectasis in lungs. Similar effects occurred in "control" pigs exposed to ~ 0.03 mg/m^3.	Frey et al. (1979) B-12
HCHO ~ 0.03 (0.02)		Anethetized, with artificial ventilation	Pigs, 21.7 ± 1.4 kg, 6-8 wk	8	None. Actually this was meant to be the control group for the tests at 2.5 and 0.25 mg/m^3 levels	6 h, once	6 h	Significant decrease in lung compliance value from beginning of study to end. Blood gas values fluctuated but did not change significantly. Slight interstitial edema, emphysema, and atelectasis in lungs.	Frey et al. (1979) B-12

TABLE III-15. DOGS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 4.6 ± 0.4	50% 77 ± 2°F	Inhalation chamber (modified Rochester-type) Air flow 1.2 m^3/min	Dogs, purebred beagle	2 M	Not given	Continuous for 90 d	90 d	No deaths. Hematologic values were normal. Lungs showed varying degrees of interstitial inflammation.	Coon et al. (1970) B-12

TABLE III-16. MONKEYS--REPEATED DOSE AND CHRONIC EXPERIMENTAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 4.6 ± 0.4	50% 77 ± 2°F	Inhalation chamber (modified Rochester-type) Air flow 1.2 m³/min	Squirrel monkey	3 M	Not given	Continuous for 90 d	90 d	No deaths. Hematologic values were normal. Lungs showed varying degrees of interstitial inflammation.	Coon et al. (1970) B-12
HCHO 3.75 (3)		Inhalation	Monkeys	6 M	6 M	22 h/d 7 d/wk 6 mo	6 mo	Nasal discharge	Clary (1980) B--
HCHO 1.25 (1)		Inhalation	Monkeys	6 M	6 M	22 h/d 7 d/wk 6 mo	6 mo	Nasal discharge. No adverse effects noted on pathological evaluation.	Clary (1980) B--
HCHO 0.25 (0.2)		Inhalation	Monkeys	6 M	6 M	22 h/d 7 d/wk 6 mo	6 mo	No adverse effects noted while exposed or on pathological evaluation.	Clary (1980) B--

TABLE III-17. SUMMARY OF ANIMAL EXPOSURES TO FORMALDEHYDE (HCHO)

Level (mg/m^3)	Time	Species	Effects
6,330-9,630	~ 3.5 h	CAT	Immediate physical discomfort, death near end of exposure.
820-2,010	4.6-8.6 h	CAT	Immediate discomfort, respiratory difficulties, dyspnea, death in 4 to 6 d.
600-1,700	30 min	RAT	LD_{50}: 1,000 mg/m^3.
900	2 h	MUS	Death from massive pulmonary hemorrhage and edema.
712	4 h	HAM	Exfoliation of 34 to 100% of trachea cells.
312	1 h/d, 1-15 d	HAM	Histologic and cytologic changes in tracheobronchial cells, recovery 2 to 6 wk.
260	3.5 h	CAT	Discomfort, respiratory difficulties.
200	1 h/d, 3 d/wk, 4 wk	MUS	Death of 30%, metaplasia and hyperplasia of tracheobronchial epithelium.
140	2 h/d, 4 d	MUS	No significant effect.
50-150	1 h/d, 3 d/wk, 35 wk	MUS	Weight gain normal, some basal-cell hyperplasia and squamous-cell metaplasia of tracheobronchial epithelium.
10-100	40-60 d	RAT	HCHO level in blood increased 5X. Eye and nose discomfort, lower body weight and relative liver weight, increased lung defense cells.
13-63	1 h	GPG	Significant changes in lung functions; limited or no recovery at 1 h post-exposure.

(Continued)

TABLE III-17. (continued)

Level (mg/m^3)	Time	Species	Effects
12.5-63	4-24 h	RAT	Range of concentrations causing beginning toxic effects, significantly increased alkaline phosphatase activity of liver, both increased and decreased phagocytic activity of lung macrophage cells, and slight blood changes.
62.5	once/wk 17 wk	HAM	No effect.
31.2	5 h, twice	HAM	Cell damage and repair, primarily in turbinates; some adaptation to irritant effects.
~ 25	24 h	RAT	Decreased phagocytic activity of lung macrophage cells.
17-19	6 h/d, 24 mo	RAT MUS	Weight loss, deaths, squamous or epithelial metaplasia, hyperplasia, and carcinomas in nasal cavity.
10-16	10 min	MUS	Respiration rate decreased 66 to 77%.
15	39 h	GPG	Effect on blood cholinesterase and leukocytes.
12.5	5 d/wk "lifetime"	HAM	Decreased survival time; no effect on nasal epithelium.
~ 12.5	4 h/d, 5 d/wk, 13 wk	GPG	Significant changes of biochemical indexes in lung, liver, and kidneys.
12.5	5 h	HAM	Little cell damage and repair in nasal turbinates and trachea.
3-8	4 h, 1-10X	HAM	Damage to airway cells, exfoliation of tracheal and bronchial cells.

(Continued)

TABLE III-17. (continued)

Level (mg/m^3)	Time	Species	Effects
2.6-7	6 h/d, 5 d/wk, 24 mo	RAT	Decreased weight, ~ 5% deaths, dysplasia, metaplasia, and carcinoma of nasal turbinates.
7	7 d	RAT	Decreased blood cholinesterase and increased leukocytes.
7	7 d - 29 d	GPG	Decreased blood cholinesterase and increased leukocytes; greater effects from continuous 7-d exposure than longer intermittent exposure.
0.7-6.5	1-1.5 h	GPG	Significant detrimental changes in lung functions.
6	3-4 min	RBT	Decreased blood pressure, heart rate, and respiratory rate.
3.5-6	10 s	RBT	Threshold of olfactory sensitivity.
5	4 h	RAT	Decreased blood pressure; neutrophilia; eosinophilia; minor irritation to lungs, spleen, and marrow.
5-6	4 h/d, 20 d	RAT	Slight effect on neuromuscular system, slightly higher preimplantation mortality of embryos, development of offspring normal except for decreased spontaneous mobility.
4.6	90 d	RBT	Blood normal, inflammation in lungs.
4.6	90 d	DOG	Blood normal, inflammation in lungs.
4.6	90 d	MKY	Blood normal, inflammation in lungs.

(Continued)

TABLE III-17. (continued)

Level (mg/m^3)	Time	Species	Effects
2-4.6	53-90 d	GPG	No deaths; slight cholinesterase and leukocyte effects; inflammation in lung, heart, and kidneys. Allergic effects appeared at 14 d.
0.7-4.5	45-90 d	RAT	Lower body weight, slight inflammation of lungs, heart, and kidneys; and decreased DNA-ase activity of liver. Change in chronaxy ratio of antagonistic muscles, mild biochemical changes in brain, liver, kidneys, and blood. In lungs, hyperemia, desquamation and proliferation of lymphohistiocytic elements.
1.6-3.8	10 min	MUS	Respiration rate decreased 26 to 53%, with or without prior exposure to HCHO.
1-4	3 h/d, 4 d	MUS	Initial respiration rate decrease of 18 to 72% at beginning of each exposure. Some recovery during exposure, less each day.
3.75	22 h/d 7 d/wk 6 mo	RAT HAM MKY	Nasal discharge in MKY; decreased weight gain in RAT.
2-3.5	10 s - 10 min	RBT	Disturbance in nervous system responses.
2.5	6 h	PIG	No change in lung function, but moderate morphologic changes, more so in dorsal than ventral section. Changes included desquamation, interstitial edema, emphysema, and atelectasis.
0.6-2.5	1-4 h	RAT	Depression of nasal sensory response, partial recovery within 1 h.

(Continued)

TABLE III-17. (continued)

Level (mg/m^3)	Time	Species	Effects
1-2	4 h	RAT	No effect.
1.25	22 h/d 7 d/wk 6 mo	RAT HAM MKY	Nasal discharge in MKY; no other effects.
1.0	8 wk	RAT	Significant changes in ascorbic acid, nucleic acids, DNA levels in females and fetuses. Length of pregnancy increased, number of fetuses decreased, no deformities. Histochemical changes in heart, liver, and kidneys of fetuses.
1.0	8 mo	RAT	No effect on body weight or blood chemistry for either first generation or exposed offspring. Offspring had some morphological changes in lungs after 8-mo exposure.
0.69	10 min	MUS	Respiration rate decreased 14 to 16% with or without prior exposure to HCHO.
0.4-0.5	4 h/d, 19-20 d	RAT	No overall toxic effects, fetuses normal.
0.5	4-5 h/d, 4-6 mo	RAT	No effects on general health, minor changes in blood and urine parameters.
0.038-0.5	5-8 h/d, 21-28 d	GPG	No effect on general health, minor changes in blood and urine parameters, formation of antibodies.
0.06-0.39	1 h	GPG	Significant change in lung function, some recovery within 1 h post-exposure.
0.03-0.25	6 h	PIG	Change in lung function and slight lung inflammation.

(Continued)

TABLE III-17. (concluded)

Level (mg/m^3)	Time	Species	Effects
0.25	22 h/d 7 d/wk 6 mo	RAT HAM MKY	No effect.
0.1	69-90 d	RAT	Signs of beginning damage to nasal mucosa; DNA-ase activity of liver increased, spleen decreased.
0.031-0.035	90-98 d	RAT	No effect on overall health, nervous system response slowed slightly, slight inflammation areas in lungs and liver.
0.035	3-8 h/d, 6 mo	RAT	No effect in general condition, changes in metabolic processes of liver, blood changes, and testicular biochemical changes. Decreased sperm mobility.
0.012	8-12 wk	RAT	No effect on overall health, nervous system slowed slightly, slight inflammation in areas of lungs. Biochemical changes in liver of female and fetuses, increased length of pregnancy, decreased number of fetuses, no deformities. Histochemical changes in heart and kidneys of fetuses.
0.011	7-8 h/d, 21-30 d	GPG	Blood unaffected, phagocytic activity increased, formation of antibodies; when stressed 2 mo later by hypoxia, immune response and phagocytic activity adversely affected.

SECTION IV

EXPERIMENTAL HUMAN INHALATION EXPOSURES

Table IV-1 describes acute laboratory human exposures to formaldehyde. In the Summary, Table S-2 condenses all the information regarding experimental human exposure, from about 17 mg/m^3 to 0.0024 mg/m^3. The American Conference of Governmental Industrial Hygienists gives 3.0 mg/m^3 as the time-weighted-average threshold limit value (ACGIH, 1980).

TABLE IV-1. HUMANS--ACUTE EXPERIMENTAL INHALATION EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 17.3 (13.8)	Inhalation chamber	12 M, 18-45 y; all exposed simultaneously	Controls used; no number given	30 min	Not given	Nasal and eye irritation when first entering chamber, continued mild lacrimation. Eye irritation wore off after 10 min in chamber.	Sim and Pattle (1957) B-9
HCHO 1-9.6						Irritation of the mucous membranes of the eyes and upper respiratory tract.	Lazarev (1965); cited in Zaeva et al. (1968) B-5
HCHO 6.25 (5)	Eye goggles, static flow conditions	13-20, for a total of 27 exposures	Served as own controls	5 min (up to 3 exposures)	Not given	18 positive responses (of 27) indicating moderate or severe irritation to the eyes.	Stephens et al. (1961) A-9
HCHO 5.0 (4)	Climatic chamber, 30 m³	35 M 13 F, "healthy students"	Served as own controls	7.5 min; 5 x 1.5-min exposures at 8-min intervals	39.5 min	Irritant indexes* high for each exposure, and above the values for lower exposure levels, both intermittent and continuous. Irritation of nose and throat more marked than in continuous exposure. No effects felt after 4-5 min of recovery.	Weber-Tschopp et al. (1977) A-15
HCHO 5.0 (4)	Eye goggles, dynamic flow conditions	A total of 7 exposures	Served as own controls	5 min	10 min (a 5-min pre-exposure control period)	7 of 7 positive responses indicating moderate to severe eye irritation.	Stephens et al. (1961) A-9

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* Irritant indexes included eye irritation, frequency of blinking, nasal irritation, irritation of the throat, and distress (e.g., "desire to leave the room").

(continued)

TABLE IV-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 5 (4)	Eye irritation booth connected to a chamber	Not given	Not given	5 min	5 min	Caused medium to severe eye irritation.	Schuck and Renzetti (1960) C-8 Schuck and Doyle (1959) C-8
HCHO 2.5-5.0 (2-4)	Eye goggles, static flow conditions	13-20, for a total of 47 exposures	Served as own controls	5 min (up to 4 different exposures)	Not given	16 positive responses (of 47) indicating moderate or severe eye irritation.	Stephens et al. (1961) A-9
HCHO 4.0 (3.2) Exposure concentration increased steadily to this level	Climatic chamber, 30 m^3	24 M 9 F, "healthy students"	Served as own controls	37 min	37 min	Adaptation to irritant occurred to some extent during first few minutes of exposure. Irritant indexes* rose with increasing concentration in all cases except for throat irritation. Irritation to the eyes more marked and nose and throat irritation less marked than in intermittent exposures to the same levels.	Weber-Tschopp et al. (1977) A-15
HCHO 3.75 (3)	Climatic chamber, 30 m^3	35 M 13 F, "healthy students"	Served as own controls	7.5 min; 5 x 1.5-min exposures at 8-min intervals	39.5 min	Irritant indexes* ranged from slight to strong; values above those for intermittent exposure to lower levels and continuous exposure to all levels ($\leq$ 4.0 mg/m^3). Irritation of nose and throat more marked and eye irritation less marked than in exposure to a similar level during continuously rising exposure.	Weber-Tschopp et al. (1977) A-15

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* Irritant indexes included eye irritation, frequency of blinking, nasal irritation, irritation of the throat, and distress (e.g., "desire to leave the room").

(continued)

TABLE IV-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 3.75 (3)	Eye ports in a chamber, or face masks attached to the chamber	Not given	Not given	5 min		When exposure was through the hoods, moderate to severe eye irritation occurred. When exposure was through the ports, even more severe irritation occurred, with lacrimation in > 50% of the subjects.	Renzetti and Schuck (1961) C-8
HCHO 3						Threshold of irritation.	Isachenko (1940); cited in Melekhina (1960) A-9
HCHO 2.5 (2)	Eye goggles, dynamic flow conditions	13-20, for a total of 37 exposures	Served as own controls	12 min (up to 4 exposures)	Not given	9 positive responses (of 37) indicating moderate to severe eye irritation.	Stephens et al. (1961) A-9
HCHO 2.5 (2)	Climatic chamber, 30 m^3	35 M 13 F, "healthy students"	Served as own controls	7.5 min; 5 x 1.5-min exposures at 8-min intervals	39.5 min	Irritant indexes* ranged from almost none to strong; values above those for intermittent exposures to lower levels and continuous exposure to all levels ($\leq$ 4.0 mg/m^3). Irritation of nose and throat more marked and eye irritation less marked than in exposure to a similar level during continuously rising exposure.	Weber-Tschopp et al. (1977) A-15

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* Irritant indexes included eye irritation, frequency of blinking, nasal irritation, irritation of the throat, and distress (e.g., "desire to leave the room").

(continued)

TABLE IV-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 2.5	Not given	3	Not given	Not given	Not given	No changes were noted in the frequency and rhythm of respiration at HCHO levels below this.	Melekhina (1964) A-9 Melekhina (1960) A-9
HCHO 2.0	Inhalation chamber	16	Served as own controls	5 h	7-8 h; 2-h pre-exposure period	Slight, statistically insignificant changes in airway resistance parameters: FEV_1, $FEF_{25-75\%}$, VC, and nasal pressure drop. Increased odor threshold for ethylvaleriate after 2 and 4 h of exposure. Nasal mucus flow rate was decreased in the first third of the nose, more so after 4 than after 2 h of exposure. Slight subjective discomfort (1-18 on a scale of 100), increasing to 18 by 2-3 h, then decreasing to 11 by 3-5 h of exposure. This decrease indicates that acclimatization occurred. 15/15 complained of conjunctival irritation and dryness in the nose and throat. No symptoms the following morning. No change in various performance tests (arithmetic and card punching).	Andersen (1979) A-14
HCHO 1.71	Not given	3	Served as own controls	4.5 min	15 min	Caused a sharp decrease in sensitivity to light in all subjects.	Melekhina (1964) A-9 Melekhina (1960) A-9

(continued)

TABLE IV-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 1.25 (1)	Eye goggles, static flow conditions	13-20, for a total of 75 exposures	Served as own controls	5 min (up to 8 different exposures)	Not given	6 positive responses (of 75) indicating moderate to severe eye irritation.	Stephens et al. (1961) A-9
HCHO 1.25 (1)	Climatic chamber, 30 m^3	35 M 13 F, "healthy students"	Served as own controls	7.5 min; 5 x 1.5-min exposures at 8-min intervals	39.5 min	Irritant indexes* ranged from almost none to moderate; values below all those for intermittent exposure to higher levels (2.5-5.0 mg/m^3) and above some of those for continuous exposures ($\leq$ 4 mg/m^3). Nasal irritation and general distress were greater, throat irritation equal to, and eye irritation less than that for exposure to a similar level during a continuously rising exposure.	Weber-Tschopp et al. (1977) A-15
HCHO 1.25 (1.0)	Odor test room	4 trained odor analysts	Served as own controls			Lowest concentration at which all the subjects positively recognized the odor.	Leonardos et al. (1969) A-11

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* Irritant indexes included eye irritation, frequency of blinking, nasal irritation, irritation of the throat, and distress (e.g., "desire to leave the room").

(continued)

TABLE IV-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 1.0	Inhalation chamber	16	Served as own controls	5 h	7-8 h; 2-h pre-exposure period	Slight, statistically insignificant changes in airway resistance parameters: FEV$_1$, FEF$_{25-75\%}$, VC, and nasal pressure drop. No change in the odor threshold for ethylvaleriate, or nasal mucus flow rate. Slight subjective discomfort (1-10 on a scale of 100), generally increasing for 3 h then remaining steady. Below the discomfort reported for 2.0 mg/m^3, and above that for 0.3 and 0.5 mg/m^3. 15/15 complained of conjunctival irritation and dryness of the nose throat. No complaints the following morning. No change in various performance tests (arithmetic and card punching).	Andersen (1979) A-14
HCHO 1.0	Exposure chamber with respirator helmet	8	8	10 min	Not given	Odor perception in all individuals. Two experienced upper respiratory tract irritation. Majority experienced distortions of the breathing rhythm, skin-galvanic reaction, heart action, and EEG changes in α-rhythms indicating possible development of a cortical inhibition process. There was also some involuntary muscle and eye movement. Author recommended a maximum permissible concentration of 1 mg/m^3.	Sgibnev (1968) A-7
HCHO 0.95-1.0						Slight irritating effect to the mucous membrane of the eye and to the mucosa of the upper respiratory tract.	Shifman; cited in Melekhina (1960) A-9

(continued)

TABLE IV-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.53		5 M, 18-32 y; persons most sensitive to odor of the HCHO from previous testing with larger group				Caused a statistically significant lowering of the amplitude of the total EEG and the theta rhythm in most of the subjects. Considered the threshold value for effect on electrical activity of the human brain.	Fel'dman (1972) B-7
HCHO 0.5	Inhalation chamber	16	Served as own controls	5 h	7-8 h; 2-h pre-exposure period	Slight, statistically insignificant changes in airway resistance parameters: FEV_1, VC, $FEF_{25-75\%}$, and nasal pressure drop. No change in the odor threshold for ethylvaleriate. Nasal mucus flow rate was decreased in the first third of the nose, more so after 4 than after 2 h of exposure. Very slight subjective discomfort (1-5 on scale of 100), generally increasing with time. Below the discomfort reported for exposure to 0.3, 1.0, and 2.0 mg/m³. 5/15 complained of conjunctival irritation and dryness in the nose and throat. No complaints the following morning. No change in various performance tests (arithmetic and card punching).	Andersen (1979) A-14
HCHO 0.3-0.4	Exposure chamber with respirator helmet	6	6	10 min	Not given	Three subjects perceived the odor. A change in bioelectric skin potential appeared in the majority of test subjects. "Oriented reaction*" appeared in these subjects. No other significant changes noted.	Sgibnev (1968) A-7

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* Appears to be the physiological responses to the introduction of a novel sensory element into one's immediate environment.

(continued)

TABLE IV-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Refrence and Rating
HCHO 0.3	Inhalation chamber	16	Served as own controls	5 h	7-8 h; 2-h preexposure period	Slight, statistically insignificant changes in airway parameters: FEV_1, VC, $FEF_{25-75\%}$, and nasal pressure drop. No change in the odor threshold for ethylvaleriate. Nasal mucus flow rate was decreased in the first third of the nose, more so after 4 than after 2 h of exposure. Only slight subjective discomfort was reported (1-9 on a scale of 100), generally increasing with time. Above that reported for exposure to 0.5 mg/m³, and below that for 1 or 2 mg/m³. 3/15 complained of conjunctival irritation and dryness in the nose and throat. No complaints the following morning. No change in various performance tests (arithmetic and card punching).	Andersen (1979) A-14
HCHO 0.3	Not given	3	Served as own controls	4.5 min	15 min	Caused a delay in adaptation to darkness in 2/3.	Melekhina (1964) A-9 Melekhina (1960) A-9
HCHO 0.25 (0.2)	Eye exposure, bag with controlled flow rate	10-22, 19-32-y-old	Not given	300 s, once	Not given	Threshold for eye irritation.	Okawada et al. (1979) A-11

(continued)

TABLE IV-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.2	Not given	3	Served as own controls	4.5 min	15 min	Increased sensitivity to light in 3/3.	Melekhina (1964) A-9 Melekhina (1960) A-9
HCHO 0.098		3	Served as own controls	4.5 min	15 min	Threshold of formaldehyde vapor reflex effect on the functional state of the cerebral cortex, as determined by dark adaptation (no effect on 3/3).	Melekhina (1964) A-9 Melekhina (1960) A-9
HCHO 0.090	Not given	15, 17-44 y	Served as own controls	Not given	Not given	Minimum detectable odor concentration for 4/15.	Fel'dman and Bonashevskaya (1971) A-10
HCHO 0.084		3	Served as own controls	15 min	Not given	Threshold for eliciting reflex activity in optical chronaxy.*	Melekhina (1964) A-9 Melekhina (1960) A-9
HCHO 0.080	Not given	15, 17-44 y	Served as own controls	Not given	Not given	Only 11/15 could smell this level, and it was the minimum detectable concentration for 4 of them.	Fel'dman and Bonashevskaya (1971) A-10
HCHO 0.077	Not given	28, 20-30 y, "practically healthy"	Not given	Not given	Not given	Odor threshold for persons who are most sensitive to HCHO.	Makeicheva (1978) B-9
HCHO 0.068-0.075	Not given	3	Served as own controls	15 min	Not given	Subthreshold concentration for effect on optical chronaxy* or on the rheobase.**	Melekhina (1964) A-9 Melekhina (1960) A-9

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* The chronaxy is the time required for the excitation of a nervous element by a stimulus; minimum time at which a stimulus just double the rheobase** will excite contraction of a muscle.

** The rheobase is the minimum potential of electric current necessary to produce stimulation of a nerve.

(continued)

TABLE IV-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.074	Not given	15, 17-44 y	Served as own controls	Not given	Not given	Only 7/15 could smell this level.	Fel'dman and Bonashevskaya (1971) A-10
HCHO 0.073	Not given	15, 17-44 y	Served as own controls	Not given	Not given	This was the minimum detectable level for 7/15.	Fel'dman and Bonashevskaya (1971) A-10
HCHO 0.073	Not given	28, "clinically healthy," 17-48 y	Not given	Not given	Not given	Olfactory threshold (minimum perceived concentration) for persons most sensitive to HCHO.	Fel'dman (1974) A-9 Fel'dman (1972) B-7
HCHO 0.07	Inhalation	12, 19-64 y		Not given	Not given; was repeated on 3 successive days	Odor threshold for persons most sensitive to HCHO (7/12).	Melekhina (1964) A-9 Melekhina (1960) A-9
HCHO 0.065		18 M, 17-35 y				Odor threshold for the 4 persons most sensitive to HCHO.	Takhirov (1974) B-8
HCHO 0.062	Not given	28, 20-30 y, "practically healthy"	Not given	Not given	Not given	Subthreshold level for odor detection even for persons most sensitive to HCHO.	Makeicheva (1978) B-9
HCHO 0.05$\bar{4}$		18 M, 17-35 y				Subthreshold value for odor perception even for the 4 persons most sensitive to HCHO.	Takhirov (1974) B-8

(continued)

TABLE IV-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.054	Not given	28, "clinically healthy," 17-48 y	Not given	Not given	Not given	Maximum undetectable odor concentration for the subjects most sensitive to HCHO.	Fel'dman (1974) A-9
HCHO 0.054	Not given	15, 17-44 y	Served as own controls	Not given	Not given	None could detect HCHO at this level. 7/15 subjects found this level to be the maximum undetectable odor concentration.	Fel'dman and Bonashevskaya (1971) A-10
HCHO 0.053	Not given	5 (of most sensitive from olfactory tests)	Served as own controls	20 min	35 min; 5 min before and 10 min after exposure for comparison; repeated 3-4 times at unknown intervals	Threshold concentration for EEG changes after stimulation by flashing light.	Fel'dman (1974) A-9 Fel'dman and Bonashevskaya (1971) A-10
HCHO 0.05	Inhalation	12, 19-64 y		Not given	Not given; was repeated on 3 successive days	Subthreshold concentration for olfactory recognition even in the subjects most sensitive to HCHO (7/12).	Melekhina (1964) A-9 Melekhina (1960) A-9
HCHO 0.05	Inhalation	64, 17-63-y-old				Odor threshold.	Petterson and Rehn (1977); cited in Andersen (1979) A-14
HCHO 0.046		5, with distinct α-rhythm	Not given	Not given	Not given	Elicited significant desynchronization of the α-rhythm of all subjects in the electrocortical conditioned reflex study.	Makeicheva (1978) B-9

(continued)

TABLE IV-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.04	Not given	5 M, 18-32 y (most sensitive from olfactory tests)	Served as own controls	20 min	35 min; 5 min before and 10 min after exposure for comparison; repeated 3-4 times at unknown intervals	Subthreshold concentration for EEG changes after stimulation by flashing light.	Fel'dman (1974) A-9 Fel'dman and Bonashevskaya (1971) A-10 Fel'dman (1972) B-7
HCHO 0.035		5, with distinct α-rhythm	Not given	Not given	Not given	Apparently inactive in the electrocortical conditioned reflex study. Proposed one-time MAC in atmospheric air should be at inactive level.	Makeicheva (1978) B-9
HCHO 0.029						Threshold of salivary action.	Van Ven'-yan' (1956); cited in Zaeva et al. (1968) B-5
HCHO 0.023 NO_2 0.08 Hexane 40.0	Not given	23, 14-48 y	Not given	Perhaps 7 s	Not given	17/23 detected an odor. A subthreshold mixture for the remaining 6.	Fel'dman (1974) A-9
HCHO 0.016						Threshold of irritation of the nervous system.	Van Ven'-yan' (1956); cited in Zaeva et al. (1968) B-5

(continued)

TABLE IV-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.016 NO_2 0.05 Hexane 29.0	Not given	23, 14-48 y	Not given	Perhaps 7 s	Not given	No odor was detected by any of the subjects.	Fel'dman (1974) A-9
HCHO 0.014 CO 1.4 NO_2 0.046 Hexane 23.0	Not given	5 (most sensitive from olfactory tests)	Served as own controls	20 min	35 min; 5 min before and 10 min after exposure for comparison; repeated 3-4 times at unknown intervals	Significant changes in EEG following stimulation by flashing light were observed in 4/5 subjects. Exact nature of the changes varied between individuals. The effect of this mixture appears to be simply additive.	Fel'dman (1974) A-9
HCHO 0.01 CO 1.1 NO_2 0.029 Hexane 18.3	Not given	5 (most sensitive from olfactory tests)	Served as own controls	20 min	35 min; 5 min before and 10 min after exposure for comparison; repeated 3-4 times at unknown intervals.	No effect on EEG following stimulation by flashing light was noted in any subject.	Fel'dman (1974) A-9

(continued)

TABLE IV-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.01 Acetic acid 0.006 Acetic anhydride 0.052 Acetone 0.22 Phenol 0.004 HCl 0.07	Inhalation	18 M, 17-35 y				Odor of mixture imperceptible. The index of total concentrations (the sum of the fraction of each compound present relative to its isolated threshold value) was < 0.90. Mixtures of these substances were imperceptible by odor when the index of total concentration was equal or near to 0.97-1.08, which attests to the simple summation effect, where the simultaneous presence of different atmospheric contaminants is caused by their nonspecific action at low concentrations.	Takhirov (1974) B-8
HCHO 0.0085 Acetone 0.075 Phenol 0.0027 Acetic acid 0.046 Acetic anhydride 0.031 HCl 0.072		3 M				The index of total concentration was 1.04. Caused a statistically significant change in the desynchronization of the α-rhythms of the brain cortex in all subjects.	Takhirov (1974) B-8
HCHO 0.0075						Threshold of respiratory irritation.	Van Ven'-yan' (1956); cited in Zaeva et al. (1968) B-5
HCHO 0.0075 Phenol 0.0025 Acetic acid 0.038 Acetic anhydride 0.025 HCl 0.055 Acetone 0.063		3 M				The index of total concentration was 0.86. Had no effect on the electrical activity of the brain cortex (electrocortical conditioned reflex study).	Takhirov (1974) B-8

(continued)

TABLE IV-1 (concluded)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
HCHO 0.0024						Threshold of effect on the mood of human subjects.	Van Ven'-yan' (1956); cited in Zaeva et al. (1968) B-5

SECTION V

EPIDEMIOLOGY AND RELATED HUMAN EXPOSURES

Chapter VI contains a discussion of the epidemiological studies. The Summary contains a table, S-3, condensing the better data. A discussion of on-going epidemiological studies is given in Appendix A. Studies tabulated herein are classified according to whether the exposures were occupational or of the general public.

OCCUPATIONAL EXPOSURES

Data for the occupational exposures to HCHO are given in Table V-1. The information is ordered by decreasing HCHO concentration. Maximum values determine the place in the table where ranges are given. Studies with no HCHO concentrations reported were generally placed at the end of the table. However, as with the mortician studies, when a similar study was tabulated that did report HCHO levels, the no-concentration entry immediately followed it.

The usefulness of the studies is limited by the frequent presence of confounding factors (especially dusts and phenol), the one-time measurement of HCHO levels during chronic exposure, the probable variations in HCHO level with time, and the usual lack of an adequate control or comparison group.

The general system for assigning applicability ratings to the documents as described in Figure I-1 was modified to accommodate the kinds of occupational exposures described. Studies describing long-term, nonconfounded exposure, with symptoms correlated to HCHO concentration, were rated A. Similar long-term studies, but with slightly confounded exposure or non-respiratory endpoints and symptoms measured, received B ratings. Short-term exposure studies, those with more serious confounding, those which lacked correlation with HCHO level, or those which provided no concentrations were rated C. D-ratings were given to studies which had multiple problems, or were badly confounded.

EXPOSURES OF THE GENERAL PUBLIC

Data from epidemiological studies of exposure of the general public are given in Table V-2, listed in order of decreasing HCHO concentration. The maximum concentration was used to decide placement in the table when ranges were given. Again, the studies were of limited usefulness due to lack of proper control groups, no reasonable estimates of HCHO exposure, and severe selection bias. No study received an A-rating, because they lacked chronic (in terms of the human lifespan) exposure and had only one-time HCHO measurements during an exposure in which the HCHO levels probably continuously decreased with time. Thus, dose-response relationships could not be determined. Lack of concentration information resulted in a C-rating, and combined with a lack of formal study design resulted in a D-rating.

TABLE V-1. STUDIES OF OCCUPATIONAL EXPOSURE TO FORMALDEHYDE (HCHO)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 5-78 Methanol 2.1-7.5 Ethanol 47.5-110	Workers in the formalin dept. of a sheepskin dyeing factory	99 F; 25-40-y-old; worked for 5-20 y	84 F in other shops, free of HCHO vapors	Complaints of persistent headache, vertigo, irritability, and tendency to weep. Skin temperature was measured on the forehead, chest, and forearm, and the variations between the left and right sides of the body reported. The incidence of physiological thermal asymmetry (a difference of 0.1-0.5 °C) before work was 43.3% in the exposed group and 27.2% in the controls. The incidence of pathological thermal asymmetry (0.6-2.2 °C) before work was 48.4% in the test group and 3.0% in the controls. After work, the physiological asymmetry was about equal in both groups (33% vs. 34.5% in the controls), and the pathological asymmetry increased to 60% in the test group, compared to 8.6% in the control group. The authors consider this evidence of adverse effects on the CNS, including the thermoregulatory center.	Essentially a prospective design. The exposure was confounded by the presence of ethanol and methanol vapors, and monochloroacetic acid. Comparability of the controls is not discussed.	Kamchatnov and Gavazova (1971) C-8

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
Working chamber: HCHO, avg. 0.56; 12-35 °C; relative humidity, 20-92%. Antechamber of the disinfection chamber: HCHO, 0.33-42.0. Mean concentration at 4 sites: 2.25-12.4	Workers servicing formalin vapor disinfection chambers. Various construction defects and incorrectly followed procedures allowed contamination of the air with HCHO. Most HCHO evolved while pouring the formalin. Higher HCHO concentrations were found at the ceiling than at the breathing zone and the floor. Hospital examinations were performed in 1967 and 1969.	93 (1967)	Not given	Diseases of the autonomic nervous system were observed in 24 persons; pneumosclerosis, emphysema of the lungs, and chronic bronchitis in 17; chronic sub- and atrophic pharyngitis in 13; hyperthyroidism in 5; bronchial asthma in 3; dyskinesia of the bile ducts in 5; and thrombocytopenia in 41.	Descriptive, uncontrolled study of HCHO exposure. A wide range of exposure concentrations are reported, but symptoms are not correlated to exposure levels.	Prave et al. (1972) C-7
		223 (from total of 285 workers in same department) (1969)	Not given	Diseases of the heart and vessels were observed in 41; autonomic dystonia and autonomic neuroses in 29; diseases of the liver and bile ducts, in 14; subatrophic rhinotracheolaryngitis, in 20; cerebrosclerosis, in 18; pneumosclerosis, emphysema of the lungs, chronic bronchitis, and bronchial asthma, in 5; hyperthyroidism in 2; chronic tonsillitis, in 9; chronic conjunctivitis, in 2; neuritis of the auditory nerve in 2; chronic eczema, in 2; and facial dermatitis in 1. The percent of acetylcholine decomposition was lowered to 27-35% in 23 persons and was found at the low-normal limit (36-37%) in yet another 20. In 1969, the cholinesterase activity appeared inhibited in 30.4% of the subjects with another 29.6% on the lower-normal boundary.		

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO, 0.5-16.3 (Levels of 10.6-16.3 HCHO not typical)* Phenol, 7-10	Acrylic-wool filter department workers engaged in felting and impregnating processes.	40 production line workers and supervisors < 1 y: 22.9 ± 1.1 y; 1-5 y: 29.3 ± 6 y old; > 5 y: 38.6 ± 3.0 y old. 8 former production-line workers and supervisors 38.0 ± 4.3 y old. Present-line workers had smoked much less than the never-on-line group; but all were similar in proportions of cigarette smokers, ex-smokers and non-smokers at the time of this survey.	15 never-on-line workers, 41.8 ± 3.2 y old	All present-line groups showed an excess of chronic cough or cough and phlegm. All groups (even controls, though somewhat lower %) complained of irritation of the eyes, nose, throat, lower respiratory tract, and skin. No significant differences in FVC (forced vital capacity) or FEV_1 (one-second forced expiratory volume) among any of the groups though the ≧ 1 y groups tended to have higher FVC values. After adjustment for smoking habits, the group on the present line > 5 y had significantly lower lung function values, the 1-5 y group had somewhat lower values, and the < 1 y group was very similar to the controls. Above values were for Mon. a.m. By Fri., only decreased FEV_1 occurred in the exposed groups.	Cross-sectional study. The deficiencies include: (a) small numbers of exposed and control subjects. (b) exposure measurements not made during study. (c) control subjects were exposed to resin fumes which would tend to diminish differences. Advantages of the study are the evaluation of pulmonary function by objective measures (FEV, etc.) and adjustment for smoking history. According to the authors, the similarity between controls and previous-on-line workers suggests that the chronic effects are reversible. The controls were occasionally exposed, explaining the high prevalence of acute mucous membrane irritation in that group (47-80%).	Schoenberg and Mitchell (1975) C-9

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* None of the measurements was made during this survey. They were made (in the same month) by an insurance company industrial hygienist.

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO ≤ 37.5 (≤ 30) mostly < 12.5 (mostly < 10)	Workers employed ≥ 5 y in a factory engaged mainly in making urea-HCHO resin and molding powders and some phenol-HCHO resin. Some of the men had spent some years of service away from HCHO exposure.	25 M, ages 24-61 y, 5.5-18 y employment	None	Four had shown a mild dermatitis that cleared after a few days' treatment. Six[≠] showed blood counts with a temporary reversal of the polymorphonuclear-lymphocyte ratio. In 5 cases, the ratio returned to normal a few weeks later. Four men experienced dyspnea on exertion; one had hypertension, cardiac enlargement,[*] and albuminuria; the other, bronchial asthma[**] for several years.	A descriptive summary of case reports: (a) no controls or comparison group (b) dermatological problems improved when the workers were removed from that setting, strongly implicating HCHO exposure.	Harris (1953) C-7
HCHO 25 (20)	Workers using a gas chamber to check the efficiency of a HCHO sampler (impinger-type)	Not given	None	Immediate irritation of the eyes and upper respiratory tract: lacrimation within 15-30 s, nose and throat irritation within 20-30 s, sneezing within 1-2 min. Exposure could continue "for some length of time" but was distinctly uncomfortable.	Anecdotal account.	Barnes and Speicher (1942) C-3

[≠] Only 12 of the mens' blood counts are listed as "normal." Abnormalities in white cell count were most frequent: counts of 10,000-14,900 in 10 workers and 4,500 and 4,100 in 2 others.

[*] In the tabulated results, it can be seen that 3 of the 25 men showed cardiac enlargement, but the one who suffered from dyspnea is not identified.

[**] This worker is not identified from the tabulated results either. Two workers had emphysema.

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 1.25-13.75 (1-11)	Garment industry workers using nylon treated with formaldehyde-containing flame retardants	Not given	None	Eye, nose, and throat irritation.	Historical review of an industry-side problem associated with the manufacture of flameproof fabrics. Not a formal study.	Ettinger and Jeremias (1955) C-4
HCHO 2.5-12.5 (2-10) Measurements made an unspecified length of time after the incident	Employees of an industrial garment company	10 F (6 employed in areas giving repeated values of 10-11 mg HCHO/m³)	None	Loss of consciousness shortly after starting work, 4/10 having jerking limb movements. They were immediately hospitalized. After regaining consciousness, complained of headache, nausea, dizziness, and vomiting. 1/10 continued to have tremors of the feet and legs. One required continued hospitalization. Engineer measuring the HCHO levels felt burning sensations of the eyes and nose along with a feeling of suffocation. Workers in the room at that time didn't demonstrate any detectable dislike or discomfort, indicating possible decreased susceptibility following repeated exposures.	Description of apparent acute exposure to formaldehyde fumes (3 locations gave 10-11 mg/m³). Physiologic measurements (blood or urine HCHO or formate) were not performed. The uniformity of complaints and short time period suggest a common exposure. Interesting that no one complained of eye irritation or nasal stuffiness except the environmental engineer taking the measurements. The evidence is highly suggestive for HCHO, but not causal. CO was ruled out.	Ahmad and Whitson (1973) C-4

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
	Workers in a phenol-HCHO plastics factory.	Total: ~ 34% M ~ 66% F > 55% 20-39 y	Mine workers and metallurgical workers	Loss of work capacity on the average significantly exceeded the sick rates of mine and metal workers. The sick rate was even more elevated in 1961, 1962, and 1969--years of grippe epidemics. Avg. length of illness in these years was 6.5-10.3 d.	The authors concluded that the complex of volatile products found in the air of workplaces using phenol-HCHO resins was significantly more toxic than the separate actions of phenol and HCHO. Note that the sick rates were not related to the specific exposure levels, or to duration of exposure.	Nagornyi (1977) C-5
HCHO 26-89	Formalin depot (required gas masks)					
Phenol (C_6H_5OH) 12-43; avg. 28.3	Max. concentration to which melters of phenol were exposed 2-5 times per shift for 4-6 min each time.			Sickness rate per 100 workers per year: Respiratory organ illness: 77 cases (93% due to grippe) 386 d lost (84% due to grippe).	A descriptive study, with the exposure confounded by the presence of phenol, lead, and resin dust. No controls, only a broad comparison to mine and metallurgical workers. Comparability for social factors that influence wo absence is not established. No baseline measurements that would allow workers pre-employment to serve controls. The main advantage of the study is the use of objective outcome measures, i.e., days absent, etc. Also fairly detailed description of symptoms and illness.	
HCHO avg. 5.3	Same general area. HCHO escaped from formalin metering tank.			(Nos. of cases and days lost due to grippe were 1.7-1.9 and 1.8-2.2 times higher, respectively, than in metallurgical workers.)		
Phenol 0.9-6.0; avg. 2.8 HCHO 0.9-11.5 avg. 3.9 30-35°C	Worker beside the autoclave during loading of the hardened articles.			Illness of alimentary organs (gastritis, stomach or duodenal ulcers, hepatitis, cholecystitis): 18 cases 149 d lost		
Phenol avg. 1.7 HCHO avg. 6.7	Area where articles were removed from the molds.			Diseases of blood-forming organs: 15 cases 285 d lost		
Phenol avg. 1.3 HCHO avg. 2.4	Washing department.			Skin diseases: 10 cases 61 d lost		

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
Phenol avg. 1.8 HCHO avg. 2.5	Curing department foreman.			In addition, women showed complications of pregnancy, labor, and the postnatal period.		
Phenol avg. 1.5 HCHO avg. 1.3	Pouring of resin into tank.			Various illnesses were diagnosed in 43% of the workers: Asthenic syndrome, neurosis, or neurasthenia 9.5% Autonomic polyneuralgia 5.4% Radiculitis 4% Hepatocholecystitis and cholecystitis 5.4% Chronic gastritis 4% Occupational dermatosis 2.7%		
Aerosols of lead and resin dusts also contaminated the workplace air, e.g., Pb 0.006-0.06	Casting lead molds.			Changes in blood pressure and pulse rate were observed principally in workers with different illnesses. Changes in erythrocyte sedimentation rate and in the no. of leukocytes were nearly identical in practically healthy and sick workers. Practically healthy workers complained most often of headaches (9.5%), pains in the heart region (4%), and pains in the right subcostal region. They showed dullness of the heart tones (36%), animation, lowering or inequality of the reflexes (15%), anisochorea, and tremor of the eyelids and fingers of the extended hands (2.7%).		
Resin 2.1-9.0; MAC = 6	Turning articles on lathes					
Study conducted for 12 y (1958-1969)						

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
	Workers involved in finishing textiles, in storing them in warehouses, and in selling them in shops.	80 in skin contamination study; 100 (77 F, 23 M) in blood study 20-49 y:	18 who didn't contact HCHO in their work	Finger blood samples were taken at the end of the work day (≤ 15-20 min after leaving workplace) and, for 51 workers, before the start of work. The skin was carefully washed before the blood was drawn. The HCHO concentration in the blood of the controls was not detectable in 15 and 0.06-0.09 mg% in 3.	Descriptive study. The concentrations of HCHO in the blood are positively correlated with inhalation and skin exposure. No health effects of exposed persons were recorded. Only limited controls were utilized and insufficient information is available on the duration of exposure and specific job descriptions. Skin and inhalation exposures are confounded.	Volkova and Sidorova (1971) C-9
HCHO: 5.1-8.8; avg. 6.86	Breathing zone of preparers of chemical reactants while dissolving urea-HCHO resin. Workers had ≤ 150 mg HCHO on skin of hands.	17 1 5 5 5 1		HCHO concentrations in workers' blood in mg%: < 0.06 0.06-0.10 0.11-0.20 0.21-0.40 0.41-0.70		
4-6	Working zone of tenter (drying-stretching machine). Workers had ≤ 75 mg HCHO on hands.	-				
4-5	Warehouses	-				
3.17-4.6; avg. 3.76	Specific jobs not identified.	23 3 9 5 4 2		 < 0.06 0.06-0.10 0.11-0.20 0.21-0.40 0.41-0.70		

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group Description	 Exposed	 Controls	Effects	Remarks	Reference and Rating
(Cont'd) 3-4	Finisher's working zone	-				Volkova and Sidorova (cont'd)
1.83-2.99; avg. 2.622	Specific jobs not identified.	32				
		4		< 0.06		
		9		0.06-0.10		
		11		0.11-0.20		
		5		0.21-0.40		
		3		0.41-0.70		
1-3	Zone of service of the thermal ager and the calendar.	-				
0.55-1.3; avg. 1.065	Specific jobs not identified	10				
		5		0.06-0.10		
		4		0.11-0.20		
		1		0.21-0.40		
0.31-0.42; avg. 0.384	Commercial shops		18			
			5	< 0.06		
			7	0.06-0.10		
			6	0.11-0.20		
-	Workers before daily exposure. Four of the 6 workers with HCHO in the blood worked at the tenter machine. Perhaps they carried urea-HCHO resin home on their clothes.		51	Range 0.05-0.44		
			45	Not detected.		
			1	< 0.06		
			1	0.06-0.10		
			1	0.11-0.20		
			1	0.21-0.40		
			2	0.41-0.70		
				The correlations between HCHO in the blood and in the air were significant. However, the workers exposed to the highest air concentrations of HCHO were most contaminated on the skin with HCHO.		
				Within 18 h after exposure, HCHO was usually not present in the blood.		

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 2.6-5.3 (Kazan factory no. 1) 5.4-7.5 (Kazan factory no. 2) 2.0-3.5 (Belka factory) Formic acid, MeOH, and EtOH (all at values < MAC) Dust particles 301/cm³; 87% 6 µm in diameter and 3,420/cm³ < 0.25 µm; 53% charged (31.4% positive and 21.6% negative) Temperature 16.3-21.6°C in the cold and transitional [weather] periods. Relative humidity 47-50%	"Smoothers" in the formalin shops of 3 USSR fur production plants who treated the hair coat of the hides on roller machines, regulated the heating temperature of the smoothing roller, and observed the quality. The work was monotonous, of average strenuousness, and was performed in a standing position.	41 F; 19- to 49-y-old 3-18 y of service	14 F not having contact with HCHO	Decreased O_2 saturation of the blood occurred in 64-66% of the cases, which indicated distinct insufficiency of tissue respiration. The decreases from the control values increased with increasing HCHO concentration in the workplace: 6% at the Belka factory, 17% at factory no. 1, and 23% at factory no. 2. The O_2 saturation deficit was not recovered by the following work day. Workers also showed a decrease in the pulse rate by 4-10 beats/min, and lowering of the coefficients of efficiency of the blood supply in 25-48% of the cases and also of the systolic and diastolic blood pressure. Complaints of vertigo, stimulation and noise in the ears became especially pronounced at the end of the shift. Chronoreflexometry revealed an increase in the time of reflex action in 58-66% of the cases. At the end of the shift, 66-80% of the smoothers showed a lowering of endurance by 18.4-38.6% that attested to their fatigue.	Confounded exposure.	Samitova et al. (1973) C-10

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
(Cont'd)				Body temperature was normal, but the skin became drier during the work day and its temperature (on the face, chest, and back) was lowered by the end of the day. In 59.3% of the smoothers vs. 27.2% of the controls, the temperature was higher on the right side of the body.		Samitova et al. (1973) (cont'd)
		110 F; 20- to 40-y-old; ≥ 3 y of service	124 F not having contact with HCHO	The smoothers showed a deviation from normal menstrual function in 63.08 ± 3% of the cases; 35.4 ± 9.6% of the controls showed similar changes. The incidences of algo-hypomenorrhea, hyperpolymenorrhea, algodysmenorrhea, and acrylic blood flow were 5.0 ± 4.4, 21.0 ± 8, 34.0 ± 9.6, and 2.7 ± 1% compared to 0.8 ± 0, 16.1 ± 7.2, 16.1 ± 7.2, and 24.0 ± 0 %, respectively, in the controls.		
				During pregnancy, early and late toxicoses were more frequent in the smoothers. Pregnancies were interrupted in 37.43 ± 6.1% of the smoothers and 22 ± 10% of the controls.		

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
(Cont'd)				Gynecological morbidity comprising prolapse, folding and deviation of the uterus, and benign tumors of the sex organs (no significant difference for the latter) occurred in 64.8 ± 9.6% of the smoothers and 26.6 ± 8.7% of the controls. Prolapse of the uterus and appendages occurred with similar frequency in smoothers and controls with length of service < 5 y (~ 3%), but the frequency was 12.0 ± 7% for the smoothers and 2.32 ± 0% for the controls with > 15 y of service. Prolapse of the internal sex organs occurred with ~ 9-10% frequency in smoothers and controls with < 5 y of service, but smoothers showed an incidence of 48.0 ± 1.2% compared to 6.97 ± 3.7% for the controls when both groups had > 15 y service.		Samitova et al. (1973) (cont'd)
				Varicose dilations of the leg veins were observed in 32.0 ± 1.7% of the smoothers having > 15 y of service and 2.32% of the controls with service > 15 y.		

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO range in the 6 homes: 0.11-6.58 (0.09-5.26); range of the avg. concns. of each of the homes: 0.31-1.74 (0.25-1.39)	Embalmers in 6 Detroit-area funeral homes.	7? M	None	Eye and nose burns, sneezing, coughing, and headaches. Those who spent more time embalming experienced more irritation. 3/7 had sinus or asthma problems. 2/7 suffered from dermatitis.	The environmental measures of HCHO vapors at 6 funeral homes were compared. 187 samples ranged from 0.09 to 5.26 ppm and were higher where there was no ventilation (mean 1.34) than in well-ventilated areas (mean 0.74). Seven (?) morticians were given a questionnaire on "known toxic effects of HCHO." More attention is given to the environmental measures than the recording and analyzing of health effects. There are no controls, insufficient numbers for meaningful analysis, no correlation of symptoms to varying HCHO concentrations, and a strong likelihood of interview bias (i.e., using a questionnaire listing the major known side-effects of HCHO). Symptoms recorded, however, are consistent with known acute effects of HCHO exposure.	Kerfoot and Mooney (1975) B-4

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO Not given	Deceased embalmers licensed to practice embalming in New York State between 1902 and 1979, and for whom death certificates have been found.	67 non-white M and 1,010 white M; exact length of employment or licensure unknown	Cause-specific proportionate mortality for the U.S. general population by age, sex, race, and calendar year	50% died before the age of 65. Deaths in white males showed: insignificant increases due to all malignant neoplasms and cirrhosis of the liver, significant increase due to arteriosclerotic heart disease, and significant deficits due to pneumonia and accidents. Similar results were found for non-whites. Distribution of malignant neoplasms in white males showed: significant excess skin cancer, insignificant excess of colon, kidney, brain, CNS, and lung cancer and leukemia, slight deficits of rectal and prostate cancer, and expected level of deaths due to neoplasms of the buccal cavity and pharynx. Those licensed < 35 y (time from 1st licensure to death) showed excess kidney cancer mortality. Those licensed ≥ 35 y showed excess skin cancer. Those licensed only as embalmers had significantly higher kidney and brain cancer deaths. Those also licensed as funeral directors (presumably less HCHO exposure) had no unusual mortality.	Proportionate mortality rate (PMR) analysis of morticians designed as a preliminary investigation of the chronic effects of the exposure to HCHO. The main deficiency is inherent to the use of the PMR method which ignores the population at risk. Excess proportion of deaths (i.e., from skin cancer) may only reflect a deficit in proportion of deaths from other causes. In addition, length of employment information was not available to measure or estimate exposure (length of exposure is estimated only on the basis of the 1st year licensed). No environmental measures of HCHO could be made, and embalming fluids contain a mixture of other chemicals (antiseptic solutions, dyes, deodorizers, etc.) that would further confound this study. It is interesting that skin cancer is found in embalmers only (vs. embalmers and funeral directors) and in those with > 35 y from 1st licensure to death. No stratification by birth cohort or by year of licensure was carried out to judge if significant changes had occurred over time (since study spans 1902-1979).	Walrath and Fraumeni (unpubl.) C-9

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO	A mail survey of embalmers in 20 funeral homes in Los Angeles.	57 M; avg. age of different groups was 35-40 y; avg. length of work for different groups was 11-18 y.	None	Reported symptoms: eye, skin, nose, and throat irritation, chest tightness, shortness of breath, cough, and wheezing. From respiratory questionnaires, 31/57 were in the diagnostic category of asymptomatic, 9/57 had acute bronchitis, and 17/57 had chronic bronchitis. The asymptomatic group reported a longer work history.	Deficiencies include: (1) 71% response rate (57/80). (2) No control group. (3) Opportunity for recall and questionnaire bias. (4) No exposure estimates or measurements. (5) Diagnosis of bronchitis was made by symptoms on the questionnaire.	Plunkett and Barbela (1977) C-4

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 1.5-4.5	Trim shop finishers in 2 textile companies. Work was light and done while standing, with very little movement.	130 F; 64% worked ≧ 10 y Of all of the subjects in Shumilina (1975) study, 70% were < 40-y old.	200 F (industrial goods sales persons); 54.5% worked ≧ 10 y.	Dysmenorrhea was greater in the exposed group (24.3%) than in the controls (9.2%), and most frequent in the 31 to 40-y-old women (20.7% vs. 6.7% in the controls). Hypomenstrual syndrome predominated and increased as occupational experience increased. Hyperpolymenorrhea and monophasic menstrual cycles occurred more often in the exposed group. Inflammatory genital disease (38.2% vs. 25.1% for lighter exposed group), primary sterility, and secondary sterility (15.3% vs. 6.5% for controls) were higher in the exposed group. No differences in term births or artificial abortions were reported. During pregnancy, increases in anemia, late toxicosis, hypotension, and symptoms of impending abortion (31.1% vs. 17.5 % for controls) were reported. There were increased problems during delivery and weight of neonates was lower in the exposed group. Compare with the results for exposure to 0.05-0.7 mg HCHO/m³ (Shumilina, 1975).	Comparison bias is likely, i.e., study is confounded by lack of information on comparability of cases and controls (socioeconomic status, age, race, smoking history, etc.): (a) Differences in socioeconomic status would be expected in saleswomen vs. trim shop workers (b) Lack of information on work environment of cases vs. controls, and exposure (i.e., duration of employment vs. symptoms). (c) The gynecological disorders referred to are much more common in women of lower socioeconomic status (i.e., pelvic inflammatory disease). (d) Many of the disorders are associated with personal habits (smoking, alcohol use, etc.) and nutritional status. Although the wide spectrum of gynecological disorders and complaints suggest a major comparison differerence between cases and controls (i.e., socioeconomic status, etc.), further studies would be indicated to be certain of the role of HCHO.	Shumilina (1975) B-8

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO ≤ 5.25 (≤ 4.2) concentrations independent of temperature (59-68°F) and relative humidity (36-70%). Samples collected over "a number of days."	Workers in the glue laminating business using phenol-resorcinol-HCHO adhesives.	Not given	None	Workers in the lay-up area felt that the increased incidence of accidents involving smashed fingers or hurt toes and legs was somehow partly due to the HCHO odor which sometimes bothered them in this area.	Anecdotal account. No rates, no controls or comparison group. Exposure and health effects not well correlated. Not useful.	Freeman and Grendon (1971) D-3
HCHO 1.1-4.1 (0.9-3.3)	Employees of stores in Pasadena, Calif. where texiles and synthetic fibers were sold.	Not given	None	Formaldehyde odors were distinctly noticeable, and there was mild eye irritation. There may have been some additive effect with existing local smog.	A health dept. report where HCHO levels were measured in response to customer complaints. Symptoms of the employees and/or customers were not systematically recorded and apparently were not even surveyed. Sample size is not given and no controls were utilized. Possible additive effect of smog is alluded to, but no measurements are given.	Miller and Blejer (1966) C-3

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 1.1-3.4 (0.9-2.7) Samples taken from several locations where the odor was most intense	Employees of a company manufacturing permanently pressed pants, using a cloth pretreated with urea, HCHO, and glyoxal. The process had been in use ~ 18 mo.	350 (~ 75% F)	None	The greatest irritation of the nose and throat and tearing of the eyes was felt in the areas with the largest quantities of partially completed garments. The symptoms were strongest at the beginning of the work day and after the lunch period. The effects, in their intense phase, lasted 15-20 min, then the irritation became tolerable. No conjunctivitis was found. Older workers felt "light-headed" and had a "heavy feeling" in their chest by the end of the day, lasting 1-2 h after work. Greatest discomfort during foggy, humid, or cold weather. Employees in other areas (e.g., warehouse) were unaffected. These levels were judged not to be a systemic health hazard, but changes were made to lower the levels to avoid irritation and nuisance.	Environmental survey of HCHO concentrations accompanied by an "informal medical interview." (a) The number actually interviewed is not given ("at least one worker in each operation was interviewed," not all 350 employees). (b) No quantification of symptoms is given (no. of persons/duration of symptoms is not recorded). (c) Each person interviewed was examined for the presence of conjunctivitis, but not examined at the beginning of the workday. None was found. (d) Concentrations of HCHO are not correlated to symptoms (different areas of the plant had different levels). (e) No control or comparison group is present.	Blejer and Miller (1966) C-3
HCHO 0-3.4 (0-2.7) avg. < 1.25 (avg. < 1)	Workers in 8 cutting and finishing plants handling permanent press fabrics treated with HCHO resins.	Not given; ~ 90% F	None	Heavy tearing, wheezing, excessive thirst, and poor sleep. The incidence of respiratory illness was ~ 10% higher than prior to the initiation of the permanent press process. Minimal dermatologic effects. On entering the plant, odor was immediately perceived, decreasing in intensity during the day, but just as strong at the beginning of the next day.	Heavily biased study. No measurement or even good description of health effects. Simply a survey of complaints and intermittent air measurements.	Shipkovitz (1968) C-5

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO: start of shift, 0.6; end of shift, 3.1	Workers engaged in the production of articles from phenol-HCHO resins, either from molding powders or from plastics filled with wood charcoal and cotton combings.	50: 30 pressmen 20 polishers	Not given	Disturbances were seen more often in the pressmen than in the polishers, who were exposed to a lower resin dust concentration. Respiratory Organs Five pressmen (molders) with service ≤ 2 y showed disturbance of the upper respiratory tract--chronic rhinopharyngitis. V.P. Malinina-Putsenko (1962) was cited as reporting lung pathology in such exposures, but these authors did not observe it, perhaps because the workers studied had not had service time enough to develop it. Skin Seventeen persons complained of skin changes; 7 of them had skin irritation in the forms of dermatitis and eczema. Heart Complaints of stabbing-constricting pain in the heart region were frequent (13). There was muffling of the heart tones at the tip (in 17). Half of the subjects showed a tendency toward hypotonia. Significant shifts in the EKG were not observed. Changes appeared to be connected with dysfunction of the autonomic nervous system, and as a consequence of this, with a disturbance of the biochemistry of the heart muscle, which is clinically most often manifested by muffling of tones.	HCHO exposure is confounded by the presence of phenol and resin dust. The importance of this confounding is noted as disturbances seen more frequently in pressmen exposed to higher resin dust concentrations.	Shafaiziev and Shipovskikh (1972) C-6
Phenol: start of shift around the presses, ≤ 2; end of shift, 15.6	2-5 y employment except for 1 who had worked > 10 y. Young persons predominated.					
Resin dust: concentration not given; however, dustiness also increased as the day wore on.						

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
(Cont'd)						
				Gastrointestinal tract Anacidic gastritis was observed in 11 subjects; chronic colitis, in 4; atrophic and hypertrophic gastritis, in 3; spastic colitis, in 5; disturbances in the protein-forming and antioxidant functions of the liver, in 8 (the liver pigment formation function was disturbed in only 1). Nervous system Disturbances were seen in 24 of the 30 pressmen in the forms of asthenic and neurotic syndromes and autonomic dystonia.		Shafaiziev and Shipovskikh (1972) (cont'd)

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO ~ 1.5-2.5 Wood dust > MAC by 1.5-2 times 3-y study (1972, 1974, 1975)	Practically healthy workers in a plywood-furniture plant up to 50 y old with ≥ 5 y of service. Sorters worked in 3 shifts; 2 shifts glued plywood. Heavy lifting and hauling for sorters, more mechanization for gluers.	Not given ("13,000 cases of loss of work capacity")	None	Results of physiological studies (functional condition of motor analyzer, cardiovascular system, hand resistance, and pulse frequency) agreed with the indexes of the subjective condition of the working women in the 1st and 2nd shifts. At the end of work, complaints increased about fatigue in the muscles of the hands and feet, general weakness, headache, and eye fatigue. The highest morbidity was due to colds and flu (43.4% stated in text, 46.6% in a figure). The other illnesses were of nerves and peripheral ganglia (15.2%), cardiovascular (7.3%) and skeletomuscular systems (6.5%), female reproductive system (2.3%), and miscellaneous (22.1%). In plywood production, the women showed a two-fold higher frequency than the men in loss of work capacity per 100 workers (8.1-17.9/100 vs. 3.9-7.6/100). The incidence of cardiovascular illnesses was 8.6/100 for the women and 6.1/100 for the men.	Descriptive, uncontrolled study of morbidity and loss of work. Exposure not correlated to actual work loss. Exposure was confounded by wood dust. Physiologic studies reflect the nature of the work more than exposure to HCHO.	Avdeeva et al. (1980) D-4

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
1978 reference: HCHO 2.0 (4 x MAC) Dust 10 x MAC Phenol, aldehydes, CH_3OH, cyanides, CO, etc. @ < MAC	Workers in a foundry plant that had begun 3 y before producing molding cores from cold-hardening mixtures based on a urea-HCHO resin and H_3PO_4	543 M and F	Not mentioned, but a range of values is referred to for certain lung function indexes.	The lung-function results were examined according to job, age group, length-of-service group, and sex. normal	Descriptive, essentially uncontrolled study. Outcome measures (respiration functions and pathology) were completely determined, but exposure is confounded.	Chernomorskii et al. (1978) D-9
1980 reference*: Coremaking dept.: HCHO 0.2-1.2 CH_3OH 7.6-25.3 Casting dept.: HCHO 0.1-0.4 Dust 5.6-18.5 Benzopyrene 2.4-9.9 x 10^{-5}** Knocking-out dept.: HCHO trace to 0.2 Dust 7.6-64.3 Benzopyrene 2.4-3.8	Workers were engaged in core rod forming, molding, pouring, knocking out, or trimming.			Coremakers: The inspiration volume was somewhat lowered with age. The expiration volume was constant except for the 40- to 44-y-old group. The respiratory frequency increased during lowering of the respiratory volume with increasing age and length of service. The vital capacity was 45% lower than normal in the 45- to 49-y-old group and was ~ 30% lower in groups with length of service 1, 6-10, 11-15, or 16-20 y. The minute volume was 26-69% higher than the upper limits of the age norm and 23-85% higher in practically all length-of-service groups. The maximum ventilation of the lungs was 34-46% lower than the lower limit of the age norm in all age groups. The minimal divergence from the proper value was 25% in the length-of-service group 6-10 y and the maximum was 64% in the 5-y service group.	Teplyakov et al. (1980) concluded that the exposure to the harmful gases from the use of the cold-hardening mixture for 3-4 y prior to the clinical examination in 1976 had not caused expressed pathological changes. Time of lost work capacity and morbidity were not exceptional for any one department.	Teplyakov et al. (1980) D-9

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* Use of 4-5% free urea before resin hardening by H_3PO_4 since the start of 1978 reduced the evolution of HCHO.

** MAC = 15 x 10^{-5} mg/m³.

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
(Cont'd)						
				The coremakers were judged to have stage 1 respiratory insufficiency characterized by changes of ventilation without disturbance of the arterial composition of the blood. Lung pathology was observed in 90.5% of the men and 87.0% of the women. Men (23.8 ± 9.3%) and women (8.5 ± 3.3%) of the coremakers and knocking out workers showed hypertrophy of the mucous membrane of the rear wall of the throat and hyperemia of the mucous membrane of the vocal cords. Lacrimation and sharp pain in eyes were complaints of 5.6 ± 2.7% of the coremakers. <ins>Workers in sections of pouring and knocking out</ins>: Respiratory insufficiency was more expressed in these workers, who directly contact the cold-hardening mixture and its degradation products. Lung pathology was observed on X-ray examination (see casting workers) in 85.7% and 91.7% of the men, respectively. Among those engaged in knocking out, 11.1 ± 5.2% complained of lacrimation and sharp pain in eyes. Hoarseness, dry cough, and dryness in the nasopharynx were complaints of 44.4 ± 8.3% of the men in the knocking out section (and of 38.1% of the men and 25.4% of the women in the coremaking section).		Chernomorskii et al. (1978) (cont'd)

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
(Cont'd)						
				Casting workers: X-ray examination showed deformation of the lungs, thickening and dilation of the radix pulmonis, and the presence of coarse strands to the diaphragm and periphery, etc., in 86.6% of the women and 85.3% of the men.		Chernomorskii et al. (1978) (cont'd)
				Trimmers: Lung pathology was noted in 89.5% of the women.		
				Overall: Lung pathology was observed in 95% of the cases in all production sections even in those aged 30-40 y and with 1-5 y of service.		
				The following ailments were recorded during clinical evaluations: neuroses (17.8 ± 1.6%); diseases of the nerves and peripheral ganglia (9.1 ± 1.2%); hypertonic diseases (7.0 ± 1.1%); gastritis and duodenitis (7.1 ± 1.1%); and bronchitis, emphysema, and bronchial asthma (6.1 ± 1.0%).		
				Rank of the ailments according to time of loss of work capacity: acute respiratory diseases (21.8 ± 1.8%), diseases of the nerves and peripheral ganglia (5.2 ± 0.9%), hypertonic disease (4.2 ± 0.8%), and chronic respiratory diseases (2.5 ± 0.7%).		

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 1.1-2.0 (0.9-1.6) Ammonia, "a trace"	Two workers outside of a booth where a wood pulp paper for map-making, which had been pre-treated with urea-HCHO or melamine-HCHO resin, was treated for shrinkage control. Contaminated air leaked from the booth into the workers' breathing zone. Early 1959; the U.S. Army Map Service, Far East, in Tokyo, Japan.	≧ 2	None	Workers complained of itching eyes, dry and sore throats, disturbed sleep, and unusual thirst upon awakening in the morning shortly after the process was placed in operation.	Case report of acute exposure. A question of confounded exposure (ammonia), probably not significant.	Morrill (1961) C-4

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
Wood dust, etc. HCHO 0.04-1.76; avg. 0.5 (0.03-1.41; avg. 0.40)*	Weyerhauser Company manufacturing complex in Springfield, Oregon. A total of ~ 175 workers were exposed to HCHO.	Personnel exposure evaluations: 50 (13 twice)	None. High exposure compared to low-exposure groups.	Subjects exposed to higher HCHO concentrations did not perform visual tasks significantly differently from subjects exposed to lower concentrations. The change in performance between pre-work and post-work tests did not significantly differ according to HCHO exposure. Post-work performance was more accurate than pre-work performance for all tests and most subjects, but the difference was significant at the 5% level for only the depth perception test.	Concentrations of other substances (particulates, wood dust, resin, etc.) to which the workers were exposed were not measured. Comparability of the workers in various sections of the plant is not described. Low exposures to HCHO may be slight compared to other substances in the air. The performance tests may not have been sensitive enough to discern difference in HCHO exposure level.	Wayne et al. (1976) B-9
Avg. exposures before curtailment of operations of particleboard plant due to an explosion on October 6 (entire study period was fall 1974-spring 1975) were:		Visual function tests:** 50	Included those workers exposed to ≤ 0.44 mg $HCHO/m^3$	The high-exposure group, however, performed less accurately and less quickly in the visual tests both before and after work than did the low-exposure group. The post-work improvement in performance was greater for the high-exposure group. Pre-work responses were faster than post-work responses in only the eye movement and fixation test.		
Particleboard plant, (0.66)	20-25 workers over all shifts (mainly two); avg. length of service on job, 5.9 y.					

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* Average before October 6 (0.57); after October 6 (0.19). These are results of personal samplers.

** Visual function tests were on central visual acuity, visual acuity under glare, dynamic visual activity, depth perception, peripheral vision, accommodation, eye movement and fixation, divided attention, and color vision.

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
(Cont'd)						
		Synchronized behavioral and environmental study:				
Joint finishing area (0.59) Plywood Plant (0.50)	~ 50 workers in each shift; avg. length of service on job, 4.6 y.	17 particleboard workers; 30 joint finishing dept. workers; and 16 from plywood plant	21 green end workers	The general trend toward improved visual performance after work was significant at the 1% level. The subgroup of subjects who experienced eye irritation or eye discomfort during work did not perform significantly differently from the remaining subjects.		Wayne et al. (1976) (cont'd)
Green end* (HCHO not specifically used here), (0.19) Avg. exposure after October 6 (≤ 0.04)	Other 50 workers were employed in finishing or as maintenance men, fork-lift operators, laborers, etc.	The 21- to 64-y-old workers included 4 F. Length of service on current jobs 5 mo-18 y; avg. 3.4 y.		On their medical histories, the particleboard workers reported a significantly higher previous incidence than the other subjects of the following eye symptoms: "burning or itching," "gritty or sandy sensation," and "pain or discomfort." Of the workers in the green end of the plywood plant, a significantly smaller fraction reported eye symptoms that they felt were work related. The frequency of eye symptoms on the days of the visual function tests was no greater among the more exposed than in the less exposed workers. The lowest frequency of positive responders to complaints of bodily fatigue, headache, eye discomfort, air unsatisfactory, eye fatigue, and odor were the 25% of the workers who had the highest HCHO exposures.		

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* Area where logs and undried veneer are manipulated.

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
Shops: HCHO 0.17-0.85; avg. ≤ 0.5 Warehouses: HCHO avg. 1.69	Chiefly, salespersons in fabric shops; ~ 5% of the air sampling was in warehouses. Highest HCHO levels were by the fabric cutter, the sales counter, and the stand with the fabric samples. Warehouse workers were not exposed continuously.	1,000 (30 in warehouses)	Persons working with linen-fabrics, which are not finished by chemical compounds.	All but 373 salespersons complained in a questionnaire of worsening of their feelings of well being. A total of 6,181 complaints showed that 3,237 (52.4%) were from the group employed ≤ 10 y; 2,190 (35.4%), 11-20 y; and 754 (12.2%), > 20 y. For example, the no. of complaints on the skin-irritating action of the HCHO-resin-finished fabrics was 1.8 x lower in those employed 11-20 y and almost 6 x lower in those employed > 20 y than in those salespersons employed < 10 y. With increased length of service, the complaints also changed character. Persons working in the shops longer complained less of head pain, dizziness, irritation, nose bleeds, and stomach pains but were more often troubled by cough, tickling in the nasopharynx, catarrh, poor appetite, pains in the joints and the small of the back, and decrease or increase in arterial pressure. Complaints independent of length of service were pains in the heart, mucus discharge, sleep disturbance, dyspnea, angina, and nausea.	The authors recognize that the aging factor with increasing length of service of the salespersons may have influenced the results. It would have been useful to show the changes in complaints with increasing length of service in the control group. (1) Proportionate ratios (not rates) are used to compare complaints by duration of employment. Rates are necessary to make the above inferences (i.e., no. of complaints/no. of persons < 10 y; not no. of complaints among those working < 10 y/total complaints). Fewer complaints may be present among those employed > 20 y because there are fewer persons in this category. (2) Poorly controlled. No comparability of comparison group working with other fabrics is given (i.e., age, race, years of employment, etc.). (3) Environmental measures are not correlated with symptomology of employees, although indirect association is present. Other irritants were not examined. (4) Standard epidemiologic measures are not used. (5) Mainly acute symptoms are examined. Duration of symptoms is not stated. This is especially impor-	Markova and Sautin (1975) A-7

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
(Cont'd)				From 5,105 complaints of salespersons contacting different kinds of fabrics, only 141 (2.8%) were from those salespersons in contact with linen. A very significant increase was noted in complaints of skin irritation from staple and viscose fabrics (33.2% and 21.9% vs. 1.9% for linen fabrics).	tant when examining the length of employment.	
HCHO avg. 1.28; range 1.12-1.43	Employees in a chip board plant	5, 46 to 50-y-old	None	Levels in the urine after exposure were: HCHO 0.16-0.35 mg % HCOOH 0.68-21.83 mg % Levels in the urine after a 144-h elimination period were: HCHO 0.15-0.43 mg % HCOOH 1.02-3.62 mg % (authors state that this is a "normal" level) Compare with the results for exposure to 0.78 mg/m^3 (Einbrodt et al., 1976).		Einbrodt et al. (1976) C-6
HCHO avg. 0.78; range 0.37-1.31	Medical students and a laboratory assistant	13 (12 medical students, 21-25 y; 1 laboratory preparation assistant, 50 y)	None	After a 3-h exposure, avg. levels were: blood HCHO 0.85 mg % blood HCOOH 9.4 mg % urine HCHO 0.10 mg % urine HCOOH 3.5 mg % After a 21-h elimination period, the avg. levels were: blood HCHO 0.73 mg % blood HCOOH 7.0 mg % urine HCHO 0.25 mg % urine HCOOH 5.2 mg % Compare these values with those for exposure to 1.28 mg/m^3 (Einbrodt et al., 1976).	Authors state that the results support the theory that detoxification occurs immediately after the blood absorbs the HCHO, by oxidation to HCOOH.	Einbrodt et al. (1976) C-16

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 0.05-0.7	Warehouse inspectors in a textile company. Work was light and done while standing, with very little movement.	316 F; 56.2% worked for ≥ 10 y 70% of all the subjects in Shumilina (1975) study were < 40-y-old.	200 F (industrial goods sales persons); 54.5% worked for ≥ 10 y	Various menstrual disorders were higher in the exposed group: dysmenorrhea (20.2% vs. 9.2% for controls), hyperpolymenorrhea, and monophasic menstrual cycles. Increased incidence of inflammatory genital disease and primary sterility was reported. No differences in the number of term births and artificial abortions. During pregnancy, increases in anemia, late toxicosis, and hypotension were noted. No correlation between work experience and pregnancy disorder incidence was found. There were increased problems during birth and lower neonatal weights in the exposed group. Compare with the results for exposure to 1.5-4.5 mg HCHO/m^3 (Shumilina, 1975).	See the 1.5-4.5 mg/m^3 entry (Shumilina, 1975).	Shumilina (1975) B-8

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 0.16-0.56 (0.13-0.45)	Customers and employees of dress stores which contain fabrics treated with HCHO-containing compounds for flame retardancy and wrinkle-proofing.	Not given	None	If the curing is not complete during the treatment process, uncombined HCHO can be left in the cloth, and later given off by the finished garment. Symptoms reported were: burning and stinging eyes, headaches, an intolerable, suffocating odor, and irritation of the nose and throat. Irritant effects sometimes reported to be stronger in the spring, perhaps due to the increased shipment of treated clothing (cotton and rayon) for the summer.	Anecdotal account of customer and employee complaints. Loosely associated with air samples and samples of wearing apparel containing measurable levels of HCHO. No quantification of complaints or no. of persons with symptoms. No controls or comparison group. Not a formal study.	Bourne and Seferian (1959) C-3
During injection, at pump: HCHO 0.4-0.5 (MAC=0.5) MeOH 2.6-10.3 (MAC=5.0) During clean-up work: HCHO 0.2-0.13 MeOH 0.14-0.8	Workers in coal mines whose air content of dust and methane was controlled by injecting a urea-HCHO resin into the coal-bearing strata. Donets Coal Basin. 1973-1975 (The major effect of the treatment was the lowering of the dustiness by 32%, but the particles 2.5-5 μm in size still comprised 70-75% of the total dust particles.)	Not given	Workers in untreated mines	Workers examined in the course of 1-3 mo after the treatment and 4 mo later did not show any differences from the norms or from the control group in the following indexes: arterial pressure, pulse rate, CO_2 content in air exhaled at rest, vital capacity of the lungs, muscular work capacity, rate of processing information, and blood analysis values.	The exposure is confounded. The number of persons and symptoms are not quantified	Gadzhiev et al. (1977) D-4

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO < 0.5 (the MAC) except where the resin is produced Phenol usually > 5 (the MAC) Cresol > MAC only in 1 case 36.4°C ≥ 70-85% relative humidity	Workers in a USSR phenol-HCHO resin plant: male and female apparatus workers, male repairmen, female lab. workers, and female preparers of the raw materials. Most of the women were molders. Lost work capacity studied for the period 1973-1975.	662, 59.1% F; since the women were older than the men, a standardization was done to eliminate the effect of the age difference on the morbidity indexes.	257 M in the instrument plant and 216 F in plant management	Exposed women generally showed significantly more morbidity than did the exposed men or the controls, especially in respiratory disease, musculoskeletal afflictions (attributed to the common cold and physical exertion), and diseases of the urogenital tract. In the exposed women, the frequency of illnesses and also the percent of multiple illnesses was higher (2.3 x higher than the controls and 1.5 x higher than the exposed men). The no. of cases (140.6) and days of lost work capacity (1,013.4) among the exposed women exceeded those of the controls by 1.5-1.6 x. The exposed men did not show significant differences from the controls.	According to the authors, the questionnaires showed that the domestic situations of the women in both the exposed and control groups were similar. However, the possibility of comparison bias (especially socioeconomic status and nutrition) between those who work in the plant and those in management would seem likely. The wide spectrum of problems in the exposed group suggests major difference in life-style and socioeconomic status between cases and controls. Griesemer et al. (1980) made the observations that no description of the methods used to determine morbidity was given and that controlled social factors may play a role, so that increases in lost workdays and evidence of respiratory and urogenital diseases do not provide definitive evidence concerning the role of HCHO, although it is suggestive.	Ischenko and Pushkina (1978) C-8

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
Ambient HCHO 0.035-0.48. Highest level reported at same time as peak symptom period. Free HCHO in fabric ranged from ~ 1.4-2.8 (1.100-1.977). Vapor discharge from fabrics reached max. of ~ 2.9 (2.345).	Garment factory workers studied during Feb. 1 to Sept. 30, 1977.	3,034	No actual control group. Comparisons made to workers in same factory during same time period of 1976 when different lot of fabric was being used.	Cutaneous and mucous membrane irritations in 1,044 (30.3%) of the workers. Irritations were: erythema of the exposed parts of the body, 29%; hyperemia of the conjunctiva, 25%; pharyngeal hyperemia and dysphonia, 20%; conjunctival hyperemia and erythema of the exposed parts of the body, 14%; pruritus with undefined cause, 12%. Approx. 25% of workers reporting irritations had morbid associations that were presumed to have triggered the occurrence of the above symptoms. These were: prior contact sensibilization, 15%; neuroses and hyperthyroidism, 12%; pharyngeal tonsillitis and chronic laryngitis, 5%; gastrohepatitis and metabolic disorders, 4%; chronic conjuctivitis or refractive defects, 4%; mycosis and psoriasis, 1%. During study period 7% of workers were diagnosed with illnesses unrelated to HCHO exposure. Compared to the year before, there was ~ 8-fold increase in incidence, frequency, and seriousness of incidences of irritation during the first 2 mo the new fabrics were used; incidences decreased but remained consistently higher through the rest of the study period compared to the previous year. A remission of symptoms occurred when the lot of fabric used during the study was replaced by other fabric.	Descriptive 2-time-period study of symptoms in workers exposed to HCHO. No exposure measurements had been made during the "control" period. Also a question of bias in the ascertainment of symptoms and signs of irritation during the exposure period.	Granati et al. (1978) B-9

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 0.116 ± 0.007 to 0.324 ± 0.02 in workplaces; 0.007 ± 0.001 to 0.046 ± 0.002 in the living quarters	Furniture store workers and persons living in apartments above them.	Not given (6 apartments were above furniture stores.)	Not given (2 apartments were not above furniture stores.)	During the sampling, most of the workers complained upon interrogation of constant headaches and irritation of the mucous membranes of the eyes. There were statistically significant changes in some indexes of the morphological composition of the blood. In 3 stores, the specific action of agglomeration of the leukocytes was 82%, 50%, and 61% compared to 12% for the control group. Upon interrogation, the inhabitants of the living quarters noted a sharp strange odor. Both adults and children noted difficulty of breathing and irritation of the mucous membranes of the eyes with the most expression in the night time and early morning hours (when the store ventilation was off).	Descriptive study of furniture store workers and 6 apartments above the store. Suspect a relatively small sample size since only 8 apartments involved. Health survey appears biased (i.e., both interviewer and interviewee bias). No measurements of health effects given. Percentages are of very small numbers. Possible confounding with phenol.	Trubitskaya (1978) C-5
HCHO 0.2 (≤ 0.16) SO_2 (≤ 0.4)	Employees exposed to gases in the kiln room of a company making ceramic cookie stamps. Employees did not "usually work in the kiln room on a regular basis during the firing of the kilns."	Not given	None	Nose and throat irritation. The investigator who entered the room during firing to check the sampling equipment "felt an immediate irritation of the nose and throat; but it went away upon leaving the room."	Although the author did not consider the exposures detrimental, he recommended a local exhaust ventilation system. After its installation, the owner reported a "tremendous improvement." Note: (a) exposure was confounded by the presence of SO_2 and phenols (b) documentation of persons exposed is not given (c) no controls or comparison group, except that people improved after increased ventilation.	Apol (1976) D--

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 0.019-0.09 (< 0.014- < 0.04) Acrolein < 0.033- <0.09 (< 0.014- < 0.04) CO (< 1-15) NO_x (0.03-0.26) SO_2 (< 0.01) Total particulates 0.09-0.26	Workers in the Run and Service Building of the Union Pacific Railroad in Pocatello, Idaho. Air measurements done on April 9-10, 1972. Medical evaluation done on April 19-20, 1972.	90 M in this building; 27 M in other areas (exposure levels of these men not given)	Results of a study of 10,000 industrial workers used for comparison to the spirometry test	Workers and some of the men taking air samples complained of burning eyes. 31/114 were classified as having symptoms of bronchitis, as determined by questionnaire. 12/114 abnormal spirograms (compared to expected 7.2), not statistically significant. No pneumoconiotic lesions were identified on chest x-ray. The conclusion was that excessive chronic respiratory disease probably does not exist.	Primarily a study of the occurrence of the gases, not a health effects survey. For the purposes of this study, the effect of HCHO is confounded by the presence of several other gases.	Apol (1973) D--

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO, Ee 0.061 En 0.025 Ca 0.046 Total mean 0.047 NH_3, Ee 0.038 En 0.089 Ca 0.057 Total mean 0.052 Resorcinol, Ee 0.153 En 0.215 Ca 0.295 Total mean 0.213 Respirable particulates, < 0.5 No statistically significant differences between exposure groups for any of these pollutants.	Workers in a tire manufacturing plant using a resin system (HR) of hexamethylenetetramine (a cyclic condensation product of HCHO and NH_3) and resorcinol.	52 Group Ee: 19 given breathing tests before and after 6 h of work with HR stock. Group En: 16 given these tests before and after the shift on days they did not work with HR stock but at jobs similar to their normal jobs.	50 Group C: matched with all workers in Group E for race, shift, sex, age, and job. Given same questionnaire and breathing tests as Group E. Group Ca comprised the 19 who were given lung function tests before and after work. 55 Group O: same age, sex, and race distribution as Group E. Selected at random from total plant population and tested the same as Groups E and C.	No statistically significant difference in chronic respiratory and cardiovascular symptoms among the groups. Self-reported symptoms were greater in Group E: itch, rash, cough, dyspnea at work, chest tightness, burning eyes, running nose, burning sensation in heart region, persistent cough and phlegm. The excess of symptoms persisted after accounting for the effects of smoking and drinking. Baseline lung function tests in Groups E, C, and O showed no differences. Group Ee showed significant decrements in lung function tests measuring "small airways" effects. These are the first effects to be observed in a "hostile" atmosphere and are reversible. No lung function decrement occurred in Group En on "nonexposure" days.	Exposure is confounded by NH_3, resorcinol, HCN, and particulates. Furthermore, duration of employment may not be comparable in these groups. Mean exposure concentrations of HCHO between HR-exposed, unexposed, and control groups were similar and it is not surprising that no differences in objective measures were noted. The authors point out the lack of difference in the baseline function tests may be due to too short an exposure time for the appearance of chronic effects, the HR system produces no chronic effect, or susceptible workers choose not to work in the HR exposed jobs.	Gamble et al. (1976) C-9

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
(Cont'd)		Higher percentage of light frequent and lower consumption ethyl alcohol drinkers than in the controls.		Respirable particulate was related to functional losses in the HR-exposed workers. Functional losses occurring over a shift were greater in the older HR-exposed workers. These workers were also classified as smokers and/or drinkers; they had acute symptoms of cough, running nose, and hoarseness.		Gamble et al. (1976) (cont'd)

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO	Workers in a plastics factory producing phenol-HCHO resin comprised:	Not given		Direct contact with phenol-HCHO powders and HCHO vapors led to simultaneous action via the respiratory tract, gastrointestinal tract, and skin.	Apparent descriptive study of the sensitizing characteristics of HCHO. Lack of controls greatly reduces the usefulness of these data. Exposure levels are not well correlated to outcome, although duration of exposure of > 5 y correlates with the frequency of "general reactions" to HCHO. Standard epidemiologic measures (i.e., rates among exposed and unexposed) are missing. There is a question of possible confounding with phenol.	Kuz'menko et al. (1975) C-4
0.025-0.036 (better ventilation; but 0.22 in March when ventilation was not used).	Molders			In 8% of the workers, clinical changes of the skin were characterized by lichenifications, erythema, cracking, and peeling.		
0.012-0.04 (Dust 3)	Preparing plant workers			Skin tests with standard allergens and 0.25% aqueous solution of HCHO showed that 22% were sensitized to HCHO.		
0.11 (poor ventilation; dust 1.6 [28 in March])	Preforming plant workers			Application of graduated doses to the skin gave not only local but in some cases within 2-3 d a general reaction in the form of headache, general weakness, poor health, and exacerbation of clinical signs of allergosis. Signs of a general reaction were observed twice as often as local changes. It appeared in persons with 5 y of service.		
0.09 (dust content 28 in March)	Mechanical treatment plant workers					
21-26°C in summer R.H. 36-56%	Workers were 21 to 45 y old, half with 4-5 y of service and half > 5 y.			In 40% of the subjects, there were noted in the blood serum some indexes characterizing the pathochemical stage of the allergic process.		

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group Description	 Exposed	 Controls	Effects	Remarks	Reference and Rating
HCHO, generally < the MAC (0.5 mg/m^3 according to Griesemer, et al., 1980; 5.0 mg/m^3 according to Zaeva et al., 1968).	Workers from 2 wood-processing concerns using urea-HCHO resins; 71.2% had worked ≤ 5 y; 26.6%, 6-10 y; and 2.2%, > 10 y	278: 102 M 176 F; 74% < 40-y-old	200 age-matched, not having HCHO exposure	The prevalence of diseases of the upper respiratory tract was 28.2-58.3% in the workers compared to 13.0% in the control group. This pathology was most prevalent in workers of the hot pressing plant where the HCHO concentration was 2.5 x that in the cold pressing plant (although still less than the MAC).	Efremov concluded that the occupational exposure to HCHO played an important role in causing functional disturbances of the nasal mucous membrane and the marked catarrhal condition of the upper respiratory tract.	Efremov (1970) A-10
				Most workers complained of lowering of the sense of smell and dryness of the nose and throat.	The Formaldehyde Panel (Griesemer et al., 1980) concluded "this report supports the hypothesis that exposure to formaldehyde may lead to chronic respiratory diseases" if it is assumed that "the age-matched controls represent an appropriate comparison group (no mention was made of matching on sex and smoking history)."	
				Subatrophic changes of the nasal mucous membrane predominated in the preparation plant (55.7%) and in the hot pressing plant (41.9% of the workers).		
				Hypertrophic changes of the nasal mucous membrane occurred in the cold pressing plant (74.8%) and in the plant processing wood-chip slabs (91.5%).		
				The prevalence of upper respiratory tract pathology was greater in workers with shorter lengths of service; e.g., the morbidity of chronic rhinitis was 15.7/100 for workers with ≤ 5 y of experience compared to 2.6-5.2/100 for workers with ≥ 6-10 y of experience. Presumably, the workers with longer service had adapted to the hazard.		

(continued)

TABLE V-1 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
cont'd						
				The highest level of prevalence of chronic rhinitis was noted in persons aged 30-59 y and more (33.3-48.0/100). Similarly, for chronic pharyngitis, the prevalence was 33.3/100 for persons ≥ 50 y.		Efremov (1970) (cont'd)
		50	20 persons without respiratory tract pathology	The absorbing function of the nasal mucous membrane was judged according to the time of appearance of mydriasis (pupillary reaction) after a plug wet with a homotropine solution was inserted in the nasal cavity. In the control group this time was 41.0 ± 4.1 min. This time was shorter, indicating accelerated absorptive capacity, in all the workers whether or not they evinced any nasal pathology. In the group of workers with chronic rhinitis, it was 28.4 min ($p < 0.001$). In the healthy workers, the time was 33.3 ± 6.6 min ($p < 0.001$ compared to the control group). The acceleration was especially intensive in the 30- to 39-y-old persons, the workers with the highest level of chronic rhinitis. In persons with 3-5 y of service, the time to the pupillary reaction was 30.0 ± 4.0 min.		

(continued)

TABLE V-1 (concluded)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
cont'd						
		100	20	The motive function of the nasal mucous membranes of exposed workers, even in those with no apparent pathology, was significantly retarded compared to that of the persons of the control group. The retardation was noted most in workers with greater length of service.		Efremov (1970) (cont'd)
		278	20	In the workers, the odor thresholds for rosemary, thymol, camphor, and tar were 2.3 x higher than those of the control group. Anosmia was observed in 19 workers. There was an increase in odor thresholds in 172 of the workers, whereas pathological changes appeared in the nasal mucous membrane of only 74.		

TABLE V-2. EPIDEMIOLOGICAL AND OTHER STUDIES RELEVANT TO FORMALDEHYDE INHALATION EXPOSURE OF THE GENERAL PUBLIC

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO avg. 2.0; range < 0.8-12.5 (avg. 1.6; range < 0.5-10) 0.5 ppm was the lower limit of detectability for the method used	Connecticut residents of houses, mobile homes, and small business and public buildings with urea-formaldehyde foam insulation installed 3 wk - 4 y (avg. 11.7 mo) earlier. Only persons making complaints to the Dept. of Health were questioned.	847	None at this time, but may be done in the future	Odor was always detected at ≥ 1.0 ppm. Odor could frequently be detected at < 0.5 ppm. 70% of the cases involving health effects claimed to have detected the odor. Only one case was found in which detectable levels of HCHO (0.7-1 ppm) caused no reported symptoms. 524/847 had symptoms: eye irritation and conjunctivitis, nose and throat irritation, respiratory symptoms, nausea, stomach problems, dizziness, rash, skin growths, fatigue, aches, and swollen glands. 52-66% of the symptoms were found in those exposed to ≥ 0.5 ppm, and 34-48% were found in persons exposed to < 0.5 ppm.	A descriptive, uncontrolled study of persons complaining to the State Health Dept. The sample was biased (self-selection bias). The described symptoms are crudely correlated to HCHO levels measured. More symptomatic persons at nondetectable levels than at levels between 0.5-10 ppm. Since the study was only conducted among those who complained, the prevalence of symptoms cannot be established. There was no real attempt to correlate dose with symptoms. It is consistent with other studies suggesting irritation of the eyes, nose, and throat at > 0.1 ppm. For further comments, see Appendix A.	Giulietti (1980) B-6
HCHO avg. 2.0; range 0.8-12.5 (avg. 1.6; range 0.5-10) These were the levels measured ~ 2 y earlier, when the avg. foam age was 11.7 mo.	Follow-up survey involving 173 complaints received > 2 y previously, and investigated then for health effects due to HCHO exposure from urea-formaldehyde foam insulation (Giulietti, 1980).	135/173 households responded to the new survey	None	Of the 138 households which were symptomatic in the original study, 110 responded to the new survey, and 72 (65%) of those still complained of irritation of the nose, head, lungs, eyes, throat, skin, and gastrointestinal tract. They felt that the symptoms had remained the same or worsened in the ~ 2 y. The avg. length of time that the foam had been in place in these houses was 2.3 ± 0.8 y. 38/110 (35%) were no longer symptomatic, for a variety of reasons including moving and removal of insulation.	A follow-up of Giulietti's 1980 study in Connecticut. Survey by self-administered questionnaire. No new HCHO measurements were made. The study suggests that the original symptoms persist in the highly biased population. No controls, but the study does suggest the need for longer-term evaluation.	Most et al. (1981) B-5

(continued)

TABLE V-2 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 8.75 (7.0)	Residents of homes with urea-formaldehyde foam insulation.	4, adults and children	None	Upper respiratory tract irritation. Odor was detected, particularly in humid weather.	See entry for 1.13-1.9 mg/m^3 (CPSC, 1978), in this table.	CPSC (1978) B-2
HCHO ≥ 6.25 (≥ 5) A one-time measurement, after the school had been closed for holidays. Building was ~ 8 mo old.	First through third grade students, in a prefabricated school, for the 8 mo after construction.	Not given	None	A "large number" of the children complained of different degrees of burning eyes, headaches, pain in the eyes, abdominal pains, nausea, vomiting, increased thirst, and apathy, and were unusually pale. Odor and symptoms were particularly strong after weekends and holidays when there was no ventilation, and when the heat was on. There was a degree of habituation (tolerance) after remaining in the building for some time. Children moved to another building had no more symptoms.	A descriptive, cross-sectional study of suspected exposure to HCHO. No controls and limited exposure measurements (one-time levels when the school was closed). Detailed quantitative measurements of symptoms were not taken. There appears to be less bias in this study since the children were having symptoms prior to the discovery and measurement of HCHO. Symptoms resolved when they moved to another school, but careful, controlled documentation is not given.	Helwig (1977) B-4
HCHO 0-6.25 (0-5)	Residents of a home with urea-formaldehyde foam insulation	Not given	None	Eye and upper respiratory tract irritation.	See entry for 1.13-1.19 mg/m^3 (CPSC, 1978).	CPSC (1978) B-2
HCHO 5.0 (4.0)	Residents of a home with urea-formaldehyde foam insulation.	3	None	Residents complained of odor and suffered from eye and respiratory tract irritation.	See entry for 1.13-1.19 mg/m^3 (CPSC, 1978).	CPSC (1978) B-2

(continued)

TABLE V-2 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 0.06-4.25 (0.05-3.40); 80% of the samples were < 0.63 mg/m³	Survey of 39 conventional homes which had urea-formaldehyde foam installed, with residents complaining of adverse health effects.	14 adult M, 18 adult F, 12 children	None	Irritation of the eyes, nose, and respiratory tract were the most frequent complaints. Drowsiness, memory lapse, chronic headache, nausea, cold, cough, and sneezing were also reported. Specific exposure levels and symptoms are given in Breysse (1978).	A series of case reports of persons complaining of HCHO exposure. Exposures were measured on an individual basis. Symptoms are quite consistent, but there is no control group and only acute effects are reported. Summaries of these data do not permit an estimate or measurement of the association between HCHO exposure and specific disease or symptom syndromes.	Breysse (1978) B-6 Breysse (1979a) B-6

(continued)

TABLE V-2 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO < 0.14-> 3.75 (< 0.11->3) Twenty-six percent of the "case-study" homes exceeded 0.8 ppm; only 2% of the "random" homes exceeded 0.8 ppm.	Residents of 105 mobile homes in Wisconsin which used particle board in the construction. Forty were randomly selected by the authors and 65 were taken from complaints received by the health department.	191	None	When age of the homes was considered, both groups were found to have the same distribution of HCHO levels (levels decrease with increasing age). So the two groups were analyzed as one. Twenty-three different adverse symptoms are reported. The most common (> 25%) being: eye and nose irritation, coughing, dry/sore throat, headache, and burning eyes. Prevalence of symptoms was lower in the random group, and the only symptom which was significantly associated with HCHO concentration was burning eyes. A model is developed predicting that 20% of adults would experience burning eyes at 0.2 ppm, which the authors recommend as the indoor HCHO standard.	A mixed survey of 65 complaining mobile home owners and an attempted cross-sectional study of 208 randomly selected mobile homes. "Complaint cases" were added to the cross-sectional study when only 50% of those contacted agreed to participate: - 65 allowed air measurements to be taken. - 40/65 (60%) of these allowed clinical information to be recorded. Thus, a heavy self-selection bias is present both for the "complaint" cases and the "random" series. There are essentially no controls (whether or not the two groups are lumped together or compared). Twenty-eight percent or 16 of the "random" group met the clinical criteria of the "complaint" series. It is difficult to interpret this in view of the selection bias due to the poor response rate. Only acute symptoms are evaluated and long-term exposures cannot be estimated from this study. The threshold recommended as a standard from this study is simply an "educated guess." The study does correlate HCHO levels to age of construction materials and this will be useful in more well-controlled studies. For further comments, see Appendix A.	Hanrahan et al. (1980?) B-6

(continued)

TABLE V-2 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO avg. ~ 1.38; range 0.38-3.88 (avg. ~ 1.1; range 0.3-3.1)	Tenants, employees, and customers of a shopping center which used urea-formaldehyde foam insulation and had been open 6 mo.	Not given	None	Complaints of eye (with occasional lacrimation), nose, and throat irritation. No skin irritation. These effects were enhanced on hot-humid days.	An environmental survey of a shopping center requested by the tenants. No information on exposed persons. Only 3 sentences on subjective symptoms, which increased on hot-humid days. The survey was performed 2 wk after the foam was removed, so that the HCHO levels are not meaningful. A new ion chromatographic system for HCHO analysis was utilized (charcoal-packed tubes).	Taft (1980) C-2
HCHO 3.75 (3.0)	Residents of a home with urea-formaldehyde foam insulation.	6	None	Complaints of eye and upper respiratory irritation, stomach cramps, fatigue, and odor were reported.	See entry for 1.13-1.19 mg/m^3 (CPSC, 1978).	CPSC (1978) B-2
HCHO 3.75 (3) The maximum level measured	Residents of apartment complex where urea-formaldehyde foam had been installed.	Not given	None	Eye irritation.	See entry for 1.13-1.19 mg/m^3 (CPSC, 1978).	CPSC (1978) B-2
HCHO 2.5 (2.0)	Residents of homes with urea-formaldehyde foam insulation.	4 adults	None	Headaches and eye and upper respiratory tract irritation were reported. Odor was detected, especially on humid days.	See entry for 1.13-1.19 mg/m^3 (CPSC, 1978).	CPSC (1978) B-2

(continued)

TABLE V-2 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 0.04-2.21 (0.03-1.77) Sixty-six percent of the samples were between 0.13 and 0.61 mg/m^3; 21% were ≥ 0.63 mg/m^3	Survey of 334 mobile homes (built with particle board or chipboard) in which one or more individuals have been experiencing health problems.	523 (240 adult F; 184 adult M; 99 children < 19-y-old)	None	58% of the adults and 41% of the children experienced eye irritation. 62% of the children and 66% of the adults reported irritation of the throat. 33% of the children complained of chronic cough or cold symptoms. Chronic headache, memory lapse, drowsiness, and chronic nausea were also reported. A few elderly persons experienced chest pains and heart attacks after moving into mobile homes. More detailed case studies of some of the incidents are given in Breysse (1977).	Descriptive summary of a series of case reports; complaints and HCHO exposure measurements were recorded. Symptoms are consistent and will permit further evaluation. However, in the absence of controls, or the ability to alter exposure to establish a dose-response relationship, only a crude association can be made. The self-selected study design further complicates this problem (i.e., random selection of mobile home owners was not done).	Breysse (1979b) B-7 Breysse (1980b) B-7
HCHO ≤ 1.88 (≤ 1.5)	Residents of homes with urea-formaldehyde foam insulation	10	None	Headache and eye and upper respiratory tract irritation reported. In some homes, odor lasted only 1-3 wk. In others, persistent intermittent odor was reported. 2/10 had no symptoms (in a home where odor disappeared 1 wk after installation).	See entry for 1.13-1.19 mg/m^3 (CPSC, 1978).	CPSC (1978) B-2
E16 HCHO 1.25 (1.0)	Residents of homes with urea-formaldehyde foam insulation.	~ 2	None	Upper respiratory tract irritation. One did not complain of any odor. The other complained of odor and symptoms immediately after installation.	See entry for 1.13-1.19 mg/m^3 (CPSC, 1978).	CPSC (1978) B-2

(continued)

TABLE V-2 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO ~ 0.25-~ 1.25 (~ 0.2-~ 1.0)	Cases of possible HCHO exposure in the home, reported to the Minnesota Department of Health.	168 (93 M + 75 F; 36 newborn to 2-y-olds, 30 3 to 13-y-olds, 102 > 13-y-olds)	None	Eye, nose, and throat irritation was reported more often in adults. Coughing, wheezing, and skin rash were reported more often in the < 13-y-old groups. Diarrhea, nausea, and vomiting were reported more often in babies. Other symptoms included respiratory problems and headache. The mean HCHO concentration in the homes of persons reporting the index symptoms (eye, nose, and throat irritation) was significantly higher than the concentration in non-symptomatic individuals' homes. Persons with history of asthma reported effects at a lower dose.	Descriptive survey of complaints of possible exposures to HCHO and in-home ambient air levels. No controls. Symptoms are not correlated to exposure levels, except to state that mean levels were higher in homes with a person reporting index symptoms (eye, nose, and throat irritation). Therefore not useful for deriving a range of concern. Few data are given. The most useful information is the documentation of changes in home HCHO with changing seasons and age of home. Only acute effects were examined, and a potential for selection bias exists.	Garry et al. (1980) B-7

(continued)

TABLE V-2 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 0.10-1.21 (0.08-0.97)	Teachers and pupils in 3 schools with HCHO-emitting chipboard in the paneling and acoustic ceilings. Duration of exposure not given	1,594	497, from schools without chipboard	Test group had significantly higher frequency of complaints for: headaches, disorders of concentration ability, dizziness, nausea, irritation of the mucosa of the nose and throat, cough, and irritation of the conjunctiva. An increase in recurrent upper respiratory tract infections also reported. In a follow-up study of 328 people, 8 mo after chipboards had been removed from the school, a decrease in all symptoms was found (30-100%)	A poorly controlled cross-sectional study of the acute effects of low levels of HCHO. Controls comprised only 1/3 the no. of cases. Comparability of the groups is not described. Controls were not utilized in the follow-up portion of the study. HCHO measurements were not made. The cases were heavily biased by the complaints from teachers and students which initiated the study. Subjective "functional" outcome would be heavily influenced by this type of bias. This study needs more objective measures (i.e., absenteeism). Duration of exposure not evaluated. Strengths of the study include the following: (1) total number of cases (2) diminished symptoms were reported after the removal of the chipboards (but environmental measurements of HCHO were not repeated) (3) respiratory complaints at low levels of HCHO were reported, and so may be useful for determining a range of concern.	Burdach and Wechselberg (1980) B-9

(continued)

TABLE V-2 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 1.13-1.19 (0.9-0.95) The maximum level measured	Residents and tenants of buildings, immediately after urea-formaldehyde foam insulation was installed	> 4	None	Eye and upper respiratory tract irritation.	A series of case reports of persons complaining of HCHO exposure. Exposure measurements were made, but: (1) no controls (2) biased sample (of complaining persons) (3) symptoms only generally described (4) other irritants were not considered The report is useful to gain an appreciation of the uniformity of complaints and the breadth of the problem.	CPSC (1978) B-2
HCHO 1.13 (0.09)	Resident of a home with urea-formaldehyde foam insulation	1 adult	None	Eye and upper respiratory tract irritation. No odor after initial installation.	See entry for 1.13-1.19 mg/m³ (CPSC, 1978).	CPSC (1978) B-2
HCHO 1.0 (0.8)	Resident of a home with urea-formaldehyde foam insulation	1 F, 51 y	None	Eye irritation.	See entry for 1.13-1.19 mg/m³ (CPSC, 1978)	CPSC (1978) B-2

(continued)

TABLE V-2 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO 0-0.98 (0-0.78)	Residents of 55 homes with urea-formaldehyde foam insulation, who voluntarily reported health problems to the New Jersey State Dept. of Health; 1-40 mo after installation	153	None	111/153 complained of some adverse health effect. The main complaints were burning or tearing of eyes, sore throat, cough, runny nose, wheezing or breathing difficulty, headaches, sleeping problems, and skin rashes. Avg. HCHO concentration generally decreased with increasing time since foam installation. Of the 15 homes sampled ≥ 4 mo after installation, 9 (60%) had HCHO levels ≥ 0.01 ppm.	Descriptive, uncontrolled survey of persons complaining due to recently installed urea-formaldehyde foam insulation. Only 22 of 55 homes had air samples taken, and despite reported symptoms 5 were negative. Problems with these data: (1) only those who complained were surveyed (biased sample) (2) no controls (symptoms may vary with age, sex, race, socioeconomic status, smoking history, season, etc.) (3) limited, crude measurements of exposure. No search for other possible irritants (4) only acute effects were evaluated. (5) symptoms not correlated to exposure levels. (6) in one of the cases where measurements were made before, air sampling showed 1.5 ppb before and negative results 2 d after installation. This highlights the need for controls of these measurement procedures. The report shows that HCHO levels diminish with time, ventilation, and the removal of foam. For further comments, see Appendix A.	Marshall (1980) B-6

(continued)

TABLE V-2 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO ≤ 0.88 (≤ 0.7)	Residents of buildings with urea-formaldehyde foam insulation	9	None	Eye and upper respiratory tract irritation and headaches. Some complained of odor, lasting a few days or a couple of months. Others noticed no odor. 2/9 had no symptoms (in a home with no odor).	See entry for 1.13-1.19 mg/m^3 (CPSC, 1978)	CPSC (1978) B-2
HCHO 0.75 (0.6) The maximum level measured	Residents of a home where urea-formaldehyde foam insulation had been installed	Not given	None	Eye irritation.	See entry for 1.13-1.19 mg/m^3 (CPSC, 1978)	CPSC (1978) B-2
HCHO 0.25-0.75 (0.2-0.6)	Residents of an apartment building built with chipboard containing formaldehyde resins	4 adults	None	Complained of burning of eyes, tearing, and coughing. After 7-h exposure to 0.78 mg/m^3, between 2.3 and 6.7 mg% formic acid (HCOOH) and between 0.06 and 0.07 mg% HCHO were found in the urine. During a 17-h recovery period, between 2.3 and 4.1 mg% HCOOH and between 0.007 and 0.12 mg% HCHO were found in the urine.	An experimental study where subjects served as their own controls to evaluate biologic measurement of HCHO and formic acid excretion after varying exposures. The study design is weak and only limited conclusions can be drawn due to: (1) too few subjects to measure individual variation. (2) no baseline measurements were made when subjects were totally unexposed. (3) acute symptoms are not well correlated to biologic measurements. (4) the proposed threshold level (0.1-0.5) is derived on the basis of the sensitivity of the tests used, not on careful measurements of health or disease outcome.	Einbrodt and Prajsnar (1978) B-6

(continued)

TABLE V-2 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO ≤ 0.63 (≤ 0.5)	Residents of buildings with urea-formaldehyde foam insulation	57 adults and children	None	Eye and upper respiratory tract irritation, headaches, sore throat, muscle aches, lung congestion, skin rash, and nausea. Each incident generally caused only 1 or 2 of the symptoms. Some noticed an odor only 1 d after foam installation. Others reported an intermittent odor lasting 5 mo. Some had complaints, but smelled no odor. A few family members had no symptoms. One family was driven from the home by the odor and symptoms. The HCHO level at that time was 18.8 mg/m³.	See entry for 1.13-1.19 mg/m³ (CPSC, 1978)	CPSC (1978) B-2
HCHO avg. 0.211 max. 0.578	Residents living ~ 250 m from a plant producing formalin	52	None	9/52 complained of irritation of the upper respiratory tract, eyes, and throat. Odor was clearly perceived by the technicians taking the air samples.	This account is just a brief section in an article on experimental exposure.	Melekhina (1964) A-9
HCHO 0.36-0.46 (0.29-0.37)	Residents of a home with urea-formaldehyde foam insulation	Not given	None	Eye and upper respiratory tract irritation.	See entry for 1.13-1.19 mg/m³ (CPSC, 1978)	CPSC (1978) B-2
HCHO 0.09-0.13 (0.07-0.10)	Residents of an apartment building constructed of formaldehyde resin chipboard.	4	None	Had complained of eye and throat irritation at 0.25-0.75 mg/m³ (see entry for those levels, Einbrodt and Prajsnar, 1978). No symptoms at these levels.		Einbrodt and Prajsnar (1978) B-6

(continued)

TABLE V-2 (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO ~ 0.08- ~ 0.13 (0.06-0.10)	Children in a school built with chipboard ceilings and some furniture and walls presumably made of HCHO-containing materials. There was constant ventilation.	37	None	No complaints were received, and there was no increase in absenteeism compared to other schools in the district. 17/37 were exposed to ~ 0.13 mg/m^3, and between 1.8 and 5.2 mg% HCOOH and up to 0.05 mg% HCHO were found in their urine. 20/37 were exposed to ~ 0.07 mg/m^3, and between 1.5 and 5.9 mg% HCOOH, and up to 0.07 mg% HCHO were found in their urine. During 24-h elimination, both groups had similar values: 17.8 mg HCOOH/24-h urine for those exposed to 0.12 mg/m^3, and 15.7 mg HCOOH/24-h urine for those exposed to 0.07 mg/m^3. Authors conclude that exposure to ≤ 0.1 ppm HCHO cannot be biologically traced.	See comments for the 0.25-0.75 mg/m^3 entry (Einbrodt and Prajsnar, 1978). This study is uncontrolled, but the report of similar absenteeism rates suggests that few acute problems may be present. This descriptive study simply sets the limits of sensitivity of of the analytical measurements.	Einbrodt and Prajsnar (1978) B-6

(continued)

TABLE V-2 (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO not given	Residents of homes insulated with urea-formaldehyde (UF) foam in the year preceding the study.	1,396 (395 households)	1,395 (400 households without UF foam)	124/395 detected an odor after the installation of the foam, lasting < 1 wk- > 1 mo. From the prevalence data for the entire study period, only asthma, wheezing or breathing difficulty, and burning skin were higher in the exposed group. Only wheezing was statistically significant. Incidence data for new symptoms occurring in the study period was significant for asthma, breathing difficulty, and burning skin. The rate of acquisition of new symptoms in the post-UF installation population was significantly (slightly) above that of the control population. There was a dose-response effect between the presence and duration of odor and an increase in the rate of new symptom acquisition. Overall rates of seeking medical attention were about the same in both groups. The persistent odor group was higher, post-insulation. 64.3% of the insulated households denied any problems which they associated with the foam.	Essentially a cross-sectional study which correlates exposure to urea-formaldehyde foam insulation to the prevalence of symptoms determined by telephone interview. Unfortunately, no environmental measurements of HCHO were made to correlate with odor perception and symptoms. Control households were well-matched by geographic location and appeared similar in socioeconomic status, family size, and percentage of smokers in the households. This study could have been designed and analyzed as a concurrent prospective study and morbidity rates determined. Unfortunately, this was not done and only simple differences in proportion of symptoms were evaluated (i.e., there was no stratification by smoking status vs. exposure to HCHO). Selective recall bias may be present in the cases due to the nature of the publicity and the telephone interviews. For further comments, see Appendix A.	Thun et al. (1980) C-13

(continued)

TABLE V-2 (concluded)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Population Group			Effects	Remarks	Reference and Rating
	Description	Exposed	Controls			
HCHO Not given	Occupants of homes insulated with urea-formaldehyde foam.	24 M, 24 F, 6-mo to 75-y-old	None	The major symptoms were: dyspnea, headache, rhinitis, eye irritation, cough, and frequent colds. Other symptoms were: rash, malaise, sore throat, and vomiting in infants < 1-y-old. Symptoms lasted at least 1 mo, and up to 4 y. Only 38% could detect the odor of HCHO, indicating olfactory accommodation.	Descriptive survey of complaints of persons contacting the Rocky Mountain Poison Center after homes had been newly insulated with HCHO foam. The lack of exposure measurements made, the brief review of acute symptoms, lack of controls, the limited nos., and the selection bias all limit the usefulness of this study. Mainly a review of other studies.	Harris et al. (1981) D-3

SECTION VI

SUMMARY OF HEALTH EFFECTS INFORMATION

This chapter provides background information on the toxicity and metabolism of HCHO and reviews the most relevant studies that were described in tabular format in Chapters II through V.

BACKGROUND

Toxicity

HCHO is a well-known toxic gas, covered in such standard works as Gosselin et al. (1976). The generally acknowledged effects of gaseous HCHO are irritation of the eyes and upper respiratory tract with edema and/or laryngospasm in severe cases. It is generally believed that the high reactivity of HCHO with amines and formation of methylol adducts with nucleic acids, histones, proteins, and amino acids account for many of the adverse effects of high concentrations such as coagulation necrosis and mutagenicity.

Systemically, HCHO decreases blood pressure and causes irregular respiration. Thus, i.v doses of $\leq$ 5 mg HCHO/kg produce primarily pressor effects in anesthetized rats; at $\overline{10}$ mg/kg, both pressor and depressor effects are manifested about equally; but at 20 mg/kg, only depressor effects such as marked bradycardia and occasional transient cardiac arrest are seen. The pressor effect is thought to be due to the release of catecholamine from the sympathetic nerve endings and the adrenal medulla (Kitchens et al.. 1976).

Metabolism

Although HCHO metabolically produced at the site of damage is generally believed to be the cause of methanol-induced retinal lesions, the only eye lesion reported from exogenous HCHO is superficial irritation and burns. The metabolism of HCHO in mammals has been summarized by Akabane et al. (1970), Kitchens et al. (1976), Griesemer et al. (1980), and, most recently, by Brooks and Reinhart (1981) in the National Research Council/National Academy of Sciences publication Formaldehyde and Other Aldehydes.

Formaldehyde is a normal metabolite along with formic acid (HCO_2H), its metabolic oxidation product, in the tetrahydrofolic acid-dependent one-carbon pool. This pool is a synthetic pathway for the addition of a single carbon group to a substrate molecule. The interconversions of labile methyl

(CH_3) groups from degradation of O-, N-, and S-methyl compounds (primarily amino acids), formic acid (as its sodium salt), and HCHO are depicted in Figure VI-1.

HCHO may be utilized in the one-carbon pool (tetrahydrofolic acid pathway), but to a greater extent is converted to S-formyl glutathione, which is oxidized by NAD. Cleavage by a thiol esterase releases formic acid and glutathione. HCHO may also be oxidized to formic acid by a nonspecific aldehyde dehydrogenase (Griesemer et al., 1980). The major pathway for formate oxidation to CO_2 is via the tetrahydrofolic acid pathway (at least in rats) (Palese and Tephly, 1975; Makar and Tephly, 1977).

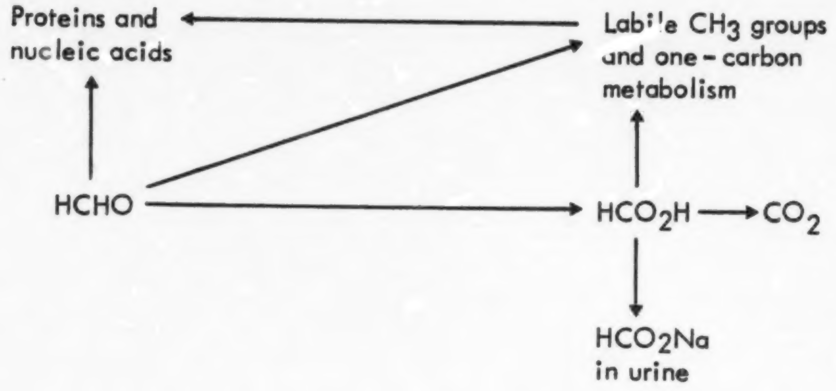
Proteins and nucleic acids
Labile CH_3 groups and one-carbon metabolism
HCHO
HCO_2H
CO_2
HCO_2Na in urine

Figure VI-1. Formaldehyde Metabolism by the Tetrahydrofolic Acid-Dependent Pathway (adapted from Griesemer et al., 1980; and Kitchens et al., 1976).

HCHO is so rapidly oxidized to formate that when measurements of the two in blood and urine are attempted after intake of HCHO or methanol, formate concentrations are always higher than those of HCHO. Sometimes HCHO is not even detected, although this may be due to a problem of analytical sensitivity. The blood half-life of HCHO in cynomolgus monkeys was estimated to be 1.5 min by McMartin et al. (1979), which agrees well with values observed in rats, guinea pigs, rabbits, and cats. However, the human data of Einbrodt et al. (1976) leads to a half-life of HCHO in blood of ~ 85 h (Dost, 1980). The plasma half-life of formate is 80-90 min (Griesemer et al., 1980).

In vitro, HCHO interferes with adenosine triphosphate (ATP) generation, uncouples oxidative phosphorylation, and possibly inhibits anaerobic glycolysis. Because the retina has a greater oxygen consumption via aerobic glycolysis in proportion to its iron content than any other tissue, HCHO is the generally accepted cause of the visual symptoms and signs observed in methanol-poisoned primates (Schneck, 1979). Perhaps the reason ocular toxicity has never been found in HCHO poisoning is because there have been far fewer cases of HCHO ingestion, or, as Gosselin et al. (1976) suggest, perhaps HCHO must be generated metabolically in the sensitive ganglion cells of the retina from methanol, never being able to reach that site when taken into the body as HCHO.

Martin-Amat et al. (cited as "to be published" by McMartin et al., 1979) have shown that formate produces ocular toxicity in the intact monkey identical to that produced by methanol. This finding, coupled with the finding that formic acid accumulation accounts for the metabolic acidosis seen in methanol poisoning, suggests that HCHO is not a major factor in methanol poisoning, at least in the monkey (McMartin et al., 1979).

The biochemical mechanisms for the differences in the toxicities of HCHO and methanol are not completely clear due to species differences, other metabolic pathways, and a variety of other complications. Regardless of the reasons why, the retinal toxicity of methanol is irrelevant to the toxicity of low levels of formaldehyde.

BIOASSAY TESTS

In vitro tests show that HCHO inhibits ciliary movement in respiratory tissue and is a weak mutagen. Only studies on respiratory tissue effects were tabulated in Chapter II. The mutagenicity of HCHO is briefly discussed here.

In vitro tests on respiratory tissues

Most of the *in vitro* tests evaluated toxic affects of HCHO and cogeners (acrolein was often compared) on respiratory tissues, the site of greatest cellular toxicity in whole-animal exposure (see Table II-1). Ciliary activity of the rabbit trachea and the clam gill was often used to quantitate effects of HCHO vapors (Cralley, 1942; Kensler and Battista, 1963; Kensler and Battista, 1966; Wynder et al., 1965). Measures were made on either the dose required to produce ciliary paralysis or on the transport rate of microscopic particles by ciliary movement in the *in vitro* preparation, before and after HCHO exposure.

Cilia of rabbit tracheas were paralyzed rapidly after HCHO exposure. Some representative doses are: 50 ppm (Dalhamn and Rosengren, 1971); 30 ppm in air or 60 ppm in buffer for 5 min (Cralley, 1942). HCHO given in eight 12-s doses, 150 mg/m^3 in each dose, produced a 50% reduction of the movement of particles in a rabbit trachea bioassay (Kensler and Battista, 1963). Kensler and Battista (1966) found HCHO was inhibitory to ciliary transport activity, but that (unlike acrolein and HCN) the effects of formaldehyde were rapidly reversible. Wynder et al. (1965) noted that HCHO had the most rapid ciliostatic effect of several aldehydes tested in a clam gill bioassay--stasis at 0.05% (500 ppm) in water--but that recovery of spontaneous activity occurred. Dalhamn and Rosengren (1971) did not look at recovery in the rabbit trachea bioassay; HCHO produced ciliostasis at 60 mg/m^3 (50 ppm). Other aldehydes were less toxic; acrolein produced ciliostasis at five times the HCHO level, and acetaldehyde effects were seen with 100 times the HCHO dose.

Other bioassays

The Formaldehyde Panel (Griesemer et al., 1980) summarized most of the available literature on the mutagenicity of HCHO, usually in the form of HCHO-food or aqueous solutions. Auerbach et al. (1977) reviewed in-depth tests with fruit flies (*Drosophila*), grasshoppers, fungi, and bacteria, and possible mechanisms of HCHO's action on DNA. HCHO vapors have seldom been tested for mutagenic effect. *Drosophila* adults exposed for ≦ 1 h and larvae exposed for ≦ 2 h to sublethal concentrations of HCHO gas showed no mutations (Auerbach, 1949; cited by Griesemer et al., 1980).

The DNA single-strand breaks and DNA-protein crosslinks in bacteria and yeast cells are the only lesions found that have been rather well characterized for HCHO. In yeast cells, the HCHO-induced single-strand breaks seem to be reparable. In both bacteria and yeast, the excision-resynthesis repair system appears to be involved in at least a fraction of formaldehyde-induced lesions (Chanet et al., 1976). In yeast, HCHO induces mitotic recombinations and a cell-cycle dependence which was demonstrated for both lethality and induction of recombination (Chanet and Von Borstel, 1979).

Effects found in cultured mammalian cells include an 8- to 10-fold increase in forward mutation frequency at the thymidine kinase locus in mouse lymphoma cells; a 1.5- to 3-fold increase in the frequency of sister chromatid exchanges in Chinese hamster ovary cells (however, Hsie et al., 1978, who were not cited by the Formaldehyde Panel, reported in a brief abstract that HCHO gave a possible false negative in the Chinese Hamster Ovary CHO/HGPRT system); and induction of unscheduled DNA synthesis in HeLa (human cervical cancer) cells by 10^{-8} to 10^{-6} *M* solutions of HCHO (Griesemer et al., 1980). A current study is attempting to correlate blood levels of HCHO with changes in human chromosomal material in cultured human lymphocytes (Anonymous, 1980c).

Griesemer et al. (1980) concluded that HCHO can be classified as a weak mutagen. Although it causes gene mutations and chromosome aberrations such as deficiencies, duplications, inversions, and translocations, dose-response relations have been poorly demonstrated. They suggested use of certain mammalian tests that would aid in the prediction of possible human genetic effects. These were the *in vitro* mammalian spot test to determine whether HCHO vapors or solutions would cause gene mutations in somatic cells that affect coat color, the heritable translocation test, and the morphological specific locus test. The latter two tests detect genetic effects in male germ cells.

Other *in vitro* test models of HCHO effects included the chorioallantoic membrane of the hen's egg, where 0.625 to 10 µg HCHO/µL (625 - 10,000 ppm or 0.0625 - 1.0%) produced hyperplasia. Comber and Grasso (1973) measured the effects of a series of chemicals on the 10-day incubated egg model, comparing toxic effects of the chemicals to that of croton oil, a potent tumor inducer. HCHO rated 3,000 on an arbitrary scale rating croton oil at 6,500. In comparison, cigarette smoke condensate rated 200; phenol, 50; and silica, < 10. Gibson (as cited in Anonymous, 1981a) speculated on HCHO's role as a promoter in his cited discussion of recent rat carcinogenicity data on the chemical.

ANIMAL EXPOSURE STUDIES

Animal studies of the effects of HCHO are detailed in a series of tables given in Chapter III and discussed below. A complete summary table is given in Chapter III, and the portion of that table concerned with levels $\leq$ 6 mg/m^3 (which is twice the threshold limit value [TLV]) is reproduced in Table S-1 in the Summary of the whole report.

Practically all the acute mouse studies (Table III-1) were 10-min exposures by Kane and Alarie (1977 and 1978). They used respiratory rate as a measure of toxic effect. HCHO, even at the lowest dose (0.41 mg/m^3), caused a decrease in rate. However, there was a threshold of sorts, in that concentrations of $\leq$ 1.54 mg/m^3 caused rate decreases of only 14 to 30%, with poor dose-response relationship, while doses of $\geq$ 1.89 mg/m^3 caused decreases of 41% or more in a dose-related fashion. Adding acrolein (another irritating aldehyde) increased the effect in a more or less additive fashion.

Kane and Alarie (1977) also did most of the repeated dose mouse studies (Table III-2). Repeated 10-min exposures (usually 4 consecutive days) produced no evidence of sensitization. However, longer exposures (3 h/d for 4 d) did provide evidence of accumulative effects. The peak decrease in respiratory rate increased on successive days and the recovery toward preexposure level (during the continued exposure) was slower each day.

Additional repeated dose and chronic studies (Table III-3) were done by Horton et al. (1963). Mice tolerated 100 mg/m^3 for 35 wk (given 1 h/d, 3 d/wk), and 35 wk at 50 mg/m^3 followed by 33 wk at 150 mg/m^3 (same schedule), with no grossly apparent toxicity, such as decreased weight gain. However, tracheobronchial epithelia showed numerous changes, especially hyperplasia and metaplasia. These potentially cancerous changes with no grossly apparent effects are disturbing. The Chemical Industry Institute of Technology (CIIT) study of rats and mice has yielded no formal publication for mice data. However, Anonymous (1981a) reported that after 24 mo at 15 ppm HCHO for 6 h/d, 5 d/wk, 2 of 85 mice had developed nasal squamous cell carcinomas.

Kilburn and McKenzie (1978) gave hamsters 4-h exposures to HCHO and HCHO-coated carbon particles (Table III-4). They were looking for damage to the airway cells and defense mechanisms. The lowest dose of HCHO alone (8 mg/m^3) was damaging to the cells. Interestingly, even 712 mg HCHO/m^3 did not cause recruitment of polymorphonucleocytes, while 4 mg HCHO/m^3 with 131 mg C/m^3 did cause such a response. Apparently the particulates (e.g., carbon soot) and the irritants activate distinct defense mechanisms. A single exposure to 12.5 mg/m^3 for 5 h caused little cell damage in nasal turbinates, trachea, or lungs, as measured by 3H-thymidine incorporation (Dalbey, 1981).

In repeated dose exposure of hamsters (Table III-5), Schreiber et al. (1979) found that up to 15 1-h exposures to 312.5 mg HCHO/m^3 caused severe cytologic changes in the tracheobronchial epithelium. These changes were reversible with complete recovery within 2 to 6 weeks. A single exposure to 31.2 mg/m^3 for 5 h caused cell damage in nasal turbinates and, to a lesser degree the trachea. A second exposure a week later indicated some adaptation to the irritant effects (Dalbey, 1981).

In the single chronic hamster exposure study, no adverse effects were reported after 6-mo exposures to 0.25, 1.25, or 3.75 mg/m^3 (Clary, 1980). There are more data from rats than from any other species. For acute exposures (Table III-6) there were a number of more or less routine toxicology studies. Skog (1950) found a 30-min LD$_{50}$ of 1,000 mg/m^3, with deaths hours to weeks after exposure due to excessive respiratory tract secretions and pulmonary edema.

Nagornyi et al. (1979) considered 18 mg/m^3 for an unstated exposure period the "acceptable limit" for pulmonary function (measured by oxygen uptake). If one relied on standard clinical chemistry parameters (e.g., SGPT), then the much higher dose of 63 mg/m^3 would be defined as the "acceptable limit." Zaeva et al. (1968) found some toxic effects (decreased blood pressure, leukocyte effects, irritation) at 5 mg/m^3, but no effects at 1-2 mg/m^3.

Two groups studied more unusual end points. Katz and Laskin (1977) studied the _in vitro_ phagocytic activity of macrophages exposed to HCHO _in vivo_; their results are difficult to interpret. Kulle and Copper (1975) looked at nasal sensory response and found decreased response even at their lowest doses, but partial recovery within an hour. The mechanism is not known, but may involve the excessive secretions as well as direct effects of HCHO on receptors.

There are many repeated dose studies on rats (Table III-7); only the more significant are discussed.

Dubreuil et al. (1976) found that continuous exposure for 3 mo to 2 mg HCHO/m^3 caused only progressive yellowing of the fur. It is not known if this represents dyeing (non-toxic effect) or a failure to groom (a toxic effect). Higher doses produced decreased weight gain, sneezing, nasal and eye discharges, and other effects.

Fel'dman and Bonashevskaya (1971) studied electrophysiological effects as well as the classical toxicological parameters. They found no effects after 3 mo at 0.012 or 0.035 mg/m^3. However, exposure to 1 mg/m^3 produced electrophysiological effects by the end of the second month and a variety of mild to moderate lesions, mostly pulmonary (desquamation of bronchial epithelium, inflammatory reactions). A higher dose (3.0 mg/m^3) produced more severe effects faster.

Sheveleva (1971) did a teratology study. She found negligible effects at 0.5 mg/m^3 and definite maternal toxicity at 5 mg/m^3. The study was not a complete, standard protocol, so some possible effects may have been overlooked.

The most significant study of the chronic exposures (Table III-8) is the excellent report of Swenberg et al. (1980)*, with rats exposed 6 h/d, 5 d/wk for 18 mo of a 24-mo study. The low dose (2.6 mg/m^3) was toxic, with decreased body weight, discolored hair, and epithelial dysplasia and/or squamous metaplasia of the nasal turbinates. The middle dose (7.0 mg/m^3) was similar, with a small incidence of rhinitis. (At 24 mo, two rats had developed squamous cell carcinomas of the nasal turbinates [NIOSH/OSHA, 1980]). The high dose of 17.6 mg/m^3 was much more toxic. Most rats had acute suppurative or seropurulent rhinitis. Squamous cell carcinomas were found in 64% of rats dying at unscheduled times (mostly after month 12) and 20% of those killed at 18 mo. (By the end of 24 mo, 95 rats exposed to the highest dose had developed nasal squamous cell carcinomas.) In recent brief reports, a study at NYU has found nasal cancers in only 10% of rats exposed to 17.5 mg/m^3 for 382 six-hour periods (Anonymous, 1981c; Anonymous, 1981d). In contrast to these two studies, Dalbey (1981) found no evidence of carcinogenicity in hamsters exposed 5 times/wk to 12.5 mg/m^3 for a "lifetime" (10-26 mo).

Gibson (as cited in Anonymous, 1981a) suggested that the nasal tumors were promoted by the tremendous cell death caused by HCHO irritation. The nature of this reaction makes the "one hit" linear model incorrect, according to Dr. Gibson. Other risk estimation techniques postulate a 1-2 ppm exposure for a 1 in 100,000 risk.

After 6 mo exposure to 0.25, 1.25, or 3.75 mg/m^3, the only adverse effect reported in rats was decreased weight gain in the highest exposure group (Clary, 1980). Nagornyi et al. (1979) found only minor (probably negligible) adverse effects in rats exposed to 0.5 mg/m^3, 5 h/d, 6 d/wk for 6 mo. Some Russian studies found small changes in various biochemical parameters after 6 mo of 3 h/d exposure to 0.035 mg/m^3 (Basmadzhieva et al., 1974), or 6 mo of 8 h/d exposure to 0.035 mg/m^3 (Davidkova and Basmadzhieva, 1979), or 4 mo of 4 h/d exposure to 0.5 mg/m^3 (Pod''yacheva, 1977). Pod''yacheva (1977) found that the effects of HCHO and phenol were additive, but the onset from combined small doses was faster.

Amdur (1960) performed many acute studies of respiratory mechanical parameters with guinea pigs breathing HCHO for 1 h (Table III-9). The lowest dose (0.06 mg/m^3) had no significant effects. The next dose (0.39 mg/m^3) caused increases in lung resistance and decreases in lung compliance with recovery in 1 h. An increase to 1.43 mg/m^3 increased breathing work and caused small, but statistically significant, increases in lung resistance 1 h after exposure. As even greater doses were used, additional parameters were affected.

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* The study, sponsored by the Chemical Industry Institute of Technology (CIIT), was performed by Battelle Columbus Laboratories. An Interagency Regulatory Liaison Group (IRLG) task force including pathologists from CPSC, DOE, EPA, NCI, and NIEHS visited CIIT in January 1980 to verify the findings. The group of pathologists in a February 1980 report concurred in general with the CIIT observations, diagnoses, and interpretations (CPSC, 1981).

Repeated dose guinea pig studies (Table III-10) varied widely in quality and relevance. Coon et al. (1970) found that 90-d continuous exposure to 4.6 mg HCHO/m^3 was toxic with interstitial inflammation of the lungs and chronic inflammation of visceral organs. Nagornyi et al. (1979) dosed guinea pigs 5 h/d, 6 d/wk for 1 mo at 0.5 mg/m^3 and found no toxicologically significant effects.

A useful rabbit study was a repeated dose study by Coon et al. (1970) (Table III-12). They found pulmonary interstitial inflammation, but no other adverse effects, in rabbits continuously exposed to 4.6 mg HCHO/m^3 for 90 d.

In the large animal studies (Tables III-13 to III-16), the most notable results were in the multi-species study of Coon et al. (1970). Beagle dogs and squirrel monkeys exposed continuously for 90 d to 4.6 mg HCHO/m^3 had varying degrees of pulmonary interstitial inflammation, like the other species they tested. In the study by Clary (1980), 6-mo exposures (22 h/d) of monkeys to 0.25, 1.25, or 3.75 mg/m^3 caused nasal discharge in the highest exposure group.

There is good evidence that the animal organism can recover from moderately irritating doses of inhaled HCHO. However, there is a limit to this recovery as shown by the progressively increasing time to recovery in studies like that of Kane and Alarie (1977) and the squamous cell carcinomas found by Swenberg et al. (1980).

There were very few interspecies studies. Nevertheless, there is no evidence of major differences.

There is a moderate amount of evidence for simple additivity with other irritants and with air pollutants having different effects.

The minimal adverse effects seem to be local irritation and subsequent tissue reactions, especially in the pulmonary system. From these studies, it appears that adverse effects appear at levels at or above 1 mg/m^3.

HUMAN EXPOSURE STUDIES

Experimental studies

Only acute inhalation studies have been reported. These are fully described in Chapter IV, Table IV-1, and summarized in Table S-2 of the report Summary.

The lowest dose at which effects have been reported is 0.0024 mg/m^3. Van Ven'-yan' as cited in Zaeva et al. (1968) stated that this level had an effect on the mood of human subjects. The same source reported 0.0075 mg/m^3

as the threshold of respiratory irritation, 0.016 mg/m^3 as the threshold of nervous system irritation, and 0.029 mg/m^3 as the threshold of salivary action. The value (if any) of these data is unknown. Other studies (Fel'dman, 1974; Takhirov, 1974) have reported on the effects of mixtures of formaldehyde with other chemicals, including nitrogen dioxide (NO_2) and hydrogen chloride (HCl). Results on odor threshold, etc., were simply additive.

A number of studies found minimal effects at about 0.05-0.08 mg/m^3 for several minutes. Russian studies (Makeicheva, 1978; Fel'dman, 1974) found that 0.046 or 0.053 mg/m^3 was sufficient to affect the electroencephalographic (EEG) response to a flashing light.

Reported odor thresholds for the most sensitive individuals include 0.05 mg/m^3 (Petterson and Rehn, 1977; as cited in Andersen, 1979), 0.065 mg/m^3 (Takhirov, 1974), 0.07 mg/m^3 (Melekhina, 1964), 0.073 mg/m^3 (Fel'dman, 1974), 0.077 mg/m^3 (Makeicheva, 1978), and 0.080 mg/m^3 (Fel'dman and Bonashevskaya, 1971). Sgibnev (1968), however, found that three of six subjects could not perceive HCHO odor at 0.3-0.4 mg/m^3.

Some electrophysiological effects have been seen at HCHO levels near 0.1 mg/m^3. Specifically, Melekhina (1964) found the threshold for affecting the optical chronaxy as 0.084 mg/m^3 and an increase in light sensitivity at 0.2 mg/m^3. However, these studies only involved 3 subjects.

Irritation thresholds are higher. Okawada et al. (1979) found an eye irritation threshold of 0.25 mg/m^3. Sgibnev (1968) found respiratory tract irritation, distortions in breathing rhythm, and other effects at 1.0 mg/m^3. Andersen (1979) reported slight discomfort and slight airway resistance changes during 5-h exposures to 0.3, 0.5, 1.0, and 2.0 mg $HCHO/m^3$. Irritation effects increase considerably in the range of 1 to 5 mg/m^3 (Stephens et al., 1961; Weber-Tschopp et al., 1977; Renzetti and Schuck, 1961). Concentrations of 5 mg/m^3 or more rapidly become unbearable, but recovery occurs 5-10 min after cessation of formaldehyde exposure (Sim and Pattle, 1957; Weber-Tschopp et al., 1977). There is evidence (Einbrodt et al., 1976) that this rapid recovery is due to rapid oxidation of the formaldehyde to formic acid.

Environmental exposures

A discussion of completed studies follows. A discussion of on-going studies is contained in Appendix A.

Occupational exposure--

Studies of occupational exposures to HCHO are fully described in Chapter V, Table V-1. The A- and B-rated studies are summarized in Table S-3 of the Summary. As is often the case, many studies are confounded by exposure to other agents, including acrolein and phenol (which have similar irritating effects). Controls generally range from poor to non-existent.

In one of the better studies, Efremov (1970) found increased prevalence of upper respiratory tract disease in workers exposed to urea-formaldehyde vapors, generally at less than the maximum allowable concentration, with reasonable dose and duration of exposure effects. Parallel effects were seen in respiratory physiology.

Because of recent reports of respiratory tumors in animals, a number of human occupational exposure studies are in progress (see Appendix A). These include mortuary workers and histotechnologists, who can have cutaneous as well as inhalation exposure. No definitive results are yet available.

Epidemiological studies--

A number of epidemiological studies have been done, primarily on the inhabitants of homes and schools with urea-HCHO insulation. These are listed in Chapter V, Table V-2. Most studies listed are defective due to no (or poor) controls, no reasonable estimates of HCHO exposure, and selection bias. Each study has been critically assessed in the Remarks column of Table V-2. The results of the better studies are given in Table S-3 of the Summary. Eye, nose, and upper respiratory tract irritation was observed for exposures to 0.211 mg HCHO/m^3 (Melekhina, 1964), but no symptoms were seen in adults or schoolchildren exposed to 0.08-0.13 mg/m^3. The most technically acceptable methodology is that of Thun et al. (1980), who surveyed homes with recently installed insulation. Although a majority of the test homes had no problems, there was an increase in wheezing and other breathing difficulties, especially in the homes and times where odors were noted. Unfortunately, no environmental measures of HCHO were made.

SECTION VII

HUMAN EXPOSURES TO FORMALDEHYDE AND RECOMMENDATIONS FOR A RANGE OF CONCERN

HUMAN EXPOSURES

Metabolic formaldehyde

Besides the normal endogenous metabolic sources of HCHO mentioned in Chapter VI, formate and HCHO can arise as metabolic products of other exogenous compounds such as acetone or methanol. In addition, *N*-demethylation of drugs such as aminopyrine or ethylmorphine or metabolism of dihalomethanes can lead to *in vivo* formation of HCHO and formate. Enzymatic hydrolysis of 5-methyltetrahydrofolate in the presence of biogenic amines and the action of mixed function oxidases on the *N*-methyl groups of various xenobiotics also produce HCHO (Griesemer et *al.*, 1980).

Public exposures to HCHO

Many researchers have found HCHO at detectable levels in the atmosphere both indoors and outdoors (see Table VII-1). Reported indoor levels range from "not detected" to 8.7 mg HCHO/m^3. The higher levels, $\geq$ 1 mg/m^3, generally are due to the use of urea-HCHO foam for insulation or polymeric materials and chipboard for construction. Energy-efficient construction (0.035-0.261 mg/m^3), use of gas stoves (0.035-0.4 mg/m^3), nearness to heavy traffic (0.051-0.106 mg/m^3), and hot, humid weather conditions (0.155 mg/m^3) all contribute to elevated indoor HCHO levels.

The highest outdoor levels (~ 0.08-2.6 mg HCHO/m^3) were generally reported near highways during rush-hour traffic (0.01-2.6) or in large cities with heavy air pollution and traffic problems, such as Los Angeles (0.04-0.16 mg/m^3) and Tokyo (0.001-0.091 mg/m^3). The lowest levels were usually reported in small towns (< 0.009 mg/m^3) and during cold weather (0.008-0.01 mg/m^3).

The level of total aldehydes in human breath has been measured: "not detected" to 0.09 mg/m^3 in smokers; "not detected" to 0.12 mg/m^3 in nonsmokers (Nefedov et al., 1969).

TABLE VII-1. REPRESENTATIVE INDOOR AND OUTDOOR ATMOSPHERIC LEVELS OF FORMALDEHYDE

Location	Concentration in mg/m^3 (ppm)	Description	Reference
Indoor	< 0.6 - 8.7 (< 0.5 - 7.0)	U.S. residences with urea-HCHO foam insulation	CPSC (1978)
	< 0.012-2.38 (< 0.01-1.90)	Interior of a new school building in West Germany, the higher levels during summer months.	Deimel (1978)
	0.08-2.24	23 Danish dwellings using chipboard	Andersen et al. (1975)
	not detected-0.97 (not detected-0.78)	U.S. residences with urea-HCHO foam installed 1->24 mo previously.	Marshall (1980)
	0.4	Kitchen (in the U.S.) with a new gas stove in use, no ventilation or hood	Hollowell et al. (1979a)
	0.080-0.261	Inside an energy-efficient house in Mission Viejo, California. Levels varied with occupancy and presence of furniture.	Hollowell et al. (1980)
	0.035-0.156 (0.028-0.125)	Inside an Energy Research Building in Ames, Iowa (see Outdoor, < 0.009, below).	Hollowell et al. (1979b) Berk et al. (1979)
	0.06-0.155 (0.048-0.124)	Living room in the summer.	Wanner (1978)
	0.106 (0.085)	First floor office, in a "traffic canyon."	Wanner et al. (1977)
	0.066 (0.053)	Suburban apartment.	Wanner et al. (1977)

TABLE VII-1 (continued)

Location	Concentration in mg/m^3 (ppm)	Description	Reference
	0.051 (0.041)	A "store and dispatch" in a residential area.	Wanner et al. (1977)
	0.04 (0.032)	Living room in the winter.	Wanner et al. (1977)
	0.035	Kitchen (in the U.S.) with new gas stove and high-speed ventilation.	Hollowell et al. (1979a)
	0.008-0.032	Interior of school in the USSR built with polymeric materials.	Trubitskaya et al. (1978)
	0.006-0.016	School in the USSR built with non-polymeric materials.	Trubitskaya et al. (1978)
Outdoor	avg. 2.6	Sidewalk and 1-2 m from road in Moscow during maximum traffic, at twilight.	Melekhina (1964)
	0.1 - 1.2	Along two USSR highways.	Prigoda (1973)
	0-0.16 (0-0.13)	Downtown Los Angeles.	Renzetti and Bryan (1961)
	0.06-0.15 (0.05-0.12)	Urban polluted air.	Stupfel (1976)
	0.005 - 0.15	A distance of 10 to 15 m from two USSR highways.	Prigoda (1973)
	0.001 - 0.091 (0.001 - 0.073)	Range of hourly values in Tokyo, during 1968 to 1976. The mean for the 9-year period was 0.009 mg/m^3.	Matsumura and Higuchi (1979)

TABLE VII-1 (concluded)

Location	Concentration in mg/m^3 (ppm)	Description	Reference
	0.01-0.09 (0.01-0.07)	South Pasadena, California.	Renzetti and Bryan (1961)
	0.04-0.08 (0.03-0.066)	Downtown Los Angeles and suburbs.	Altshuller (1978)
	0.004 - 0.025 (0.003-0.020)	Range during the summers of 1972 to 1974 in four cities in New Jersey.	Cleveland et al. (1977)
	0.016-0.019 (0.013-0.015)	Summer air.	Wanner (1978)
	0.009 - 0.018	Ohtsu area of Japan in October 1976.	Suga et al. (1978)
	0.012-0.015 (0.0093-0.012)	Near roads with varying traffic density.	Wanner et al. (1977)
	0.0062-0.0145	Sofia, Bulgaria	Kalpazanov et al. (1976)
	0.008-0.010 (0.006-0.008)	Winter air.	Wanner et al. (1978)
	< 0.009 (< 0.007)	Outdoor air in Ames, Iowa (see Indoor, 0.035-0.156, above)	Hollowell et al. (1979b) Berk et al. (1979)
	0.001-0.0068	Levels generally detected 7 to 8 m from a road in Moscow with heavy traffic at twilight. Max. of 0.017 mg/m^3.	Melekhina (1964)

Cigarette smoking

The level of HCHO found in cigarette smoke has varied with the investigator and the type of cigarette. Stupfel (1976) reported 150 mg/m^3 (120 ppm) in unspecified smoke. Newsome et al. (1965) reported 90 mg/m^3 (3.6 μg/40 mL puff) in the smoke of filtered cigarettes and 103 mg/m^3 (4.1 μg/40 mL puff) in the smoke of unfiltered cigarettes. NIOSH/OSHA (1980) reports $\leq$ 50 mg/m^3 ($\leq$ 40 ppm). NIOSH uses this figure to calculate that an individual smoking a pack of cigarettes a day would inhale 0.38 mg HCHO, whereas occupational exposure to formaldehyde at 3 ppm could result in a daily intake of 29.0 mg HCHO. From Stupfel's data it can be estimated that after each 40 mL puff containing 3.6-4.1 μg HCHO, the lung will be exposed momentarily to air containing ~ 5.1-5.8 mg HCHO/m^3 (3.6-4.1 μg/0.7 L tidal volume). This is 170-190% of the TLV (3 mg/m^3).

INTERNATIONAL STANDARDS AND RECOMMENDATIONS

A summary of regulations and recommendations is given in Table VII-2. Most of the recommendations were made by individual researchers, not regulatory or advisory agencies. The standards for occupational exposure range from 0.5 to 10 mg HCHO/m^3, for 8-h to 30-min intervals. Standards for outdoor air range from 0.01 to 0.075 mg/m^3. The American Industrial Hygiene Association (AIHA) recommended 0.12 mg/m^3 for the U.S. standard for outdoor air. Recommendations for indoor air exposure range from 0.025 to 0.62 mg/m^3.

The Committee on Toxicology of the National Research Council (NRC, 1980) concluded that "there is no population threshold for the irritant effects of formaldehyde in humans" and advised "maintaining formaldehyde at the lowest practical concentration to minimize adverse effects on public health."

NIOSH/OSHA (1980), in a Current Intelligence Bulletin, recommended that "formaldehyde be handled in the workplace as a potential occupational carcinogen." However, under orders from the Office of Health and Human Services Secretary Richard Schweiker, NIOSH has halted further distribution of that bulletin (Anonymous, 1981c).

RECOMMENDED RANGE OF CONCERN

The EPA Work Directive for this Task 6 suggested 0.03-3.0 mg HCHO/m^3 as a preliminary range of uncertainty with regard to health effects of inhaled HCHO. The threshold limit value in the United States for occupational exposures is 3.0 mg/m^3.

Experimental animals show obvious adverse effects at HCHO concentrations $\geq$ 1 mg/m^3 whether acutely or chronically exposed. In chronic studies, biochemical and inflammatory changes are seen at concentrations as low as 0.035; and 8-12 wk exposures of rats to 0.012 mg HCHO/m^3 produced such changes. Thus, a range of concern, based on animal studies would be from 0.012 to about 1 mg/m^3.

TABLE VII-2. SUMMARY OF REGULATIONS AND RECOMMENDATIONS FOR HUMAN FORMALDEHYDE EXPOSURE

HCHO Level in mg/m^3 (ppm)	Recommendation/Regulation	Type of Exposure			Reference
		Outdoor Air	Indoor Air	Occupational Air	
12.5* (10)	Promulgated ceiling exposure limit in Great Britain. Max. acceptable peak level for a total of no more than 30 min during an 8-h shift in the U.S.			X	NRC (1980) NIOSH/OSHA (1980)
6.3 (5)	Promulgated ceiling exposure limit in Japan, Finland, and U.S.			X	NRC (1980) NIOSH/OSHA (1980)
5.9 (4.7)	Promulgated ceiling exposure limit in Italy and Poland			X	NRC (1980)
5 (4)	Promulgated ceiling exposure limit in Czechoslovakia (short, single exposure) and Bulgaria			X	NRC (1980) ILO (1970)
3.8 (3)	Time-weighted avg. (TWA) promulgated by OSHA; TLV in Australia			X	NRC (1980) NIOSH/OSHA (1980) Howlett (1980)
3.1 (2.5)	Promulgated ceiling exposure limit in Sweden and Rumania			X	NRC (1980)
3 (2)	Ceiling threshold limit value (TLV) recommended by ACGIH; TLV in The Netherlands			X	NRC (1980) ACGIH (1980) Howlett (1980)
2.5* (2)	Promulgated TLV (ceiling) in Great Britain			X	Lynne (1979)

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* Note the discrepancy between the two entries.

(Continued)

TABLE VII-2 (continued)

HCHO Level in mg/m^3 (ppm)	Recommendation/Regulation	Type of Exposure			Reference
		Outdoor Air	Indoor Air	Occupational Air	
<2.5 (<2)	Recommended a TLV below this level			X	Weber-Tschopp et al. (1977)
2.1 (1.7)	Promulgated TWA (8-h) in Czechoslovakia and East Germany			X	NRC (1980) ILO (1970)
1.9 (1.5)	Proposed TLV in Italy			X	Howlett (1980)
1.2 (1)	Ceiling exposure limit recommended by NIOSH			X	NRC (1980) NIOSH/OSHA (1980)
1.2 (1)	Promulgated TWA (8-h) in Denmark and West Germany. MAC in West Germany. TLV in Poland and Yogoslavia			X	NRC (1980) Helwig (1977) Howlett (1980)
1.0 (0.8)	Promulgated ceiling exposure limit in Hungary			X	NRC (1980)
0.62 (0.5)	Recommended exposure limit in residences		X		Timm and Smith (1979)
0.62 (0.5)	Standard in The Netherlands for levels 2 wk after installation of urea-HCHO foam insulation		X		Rumack (1978)
0.12-0.62 (0.1-0.5)	Recommended exposure limit for schools and living areas		X		Einbrodt and Prajsnar (1978)
0.12-0.5 (0.1-0.4)	Recommended ceiling exposure limit in Sweden		X		NRC (1980)

(Continued)

TABLE VII-2 (continued)

HCHO Level in mg/m^3 (ppm)	Recommendation/Regulation	Type of Exposure Outdoor Air	Indoor Air	Occupational Air	Reference
0.5 (0.4)	Promulgated ceiling exposure limit in the USSR			X	NRC (1980) USSR (1972)
0.4	Proposed preliminary standard for continuous exposure, in Denmark				Andersen (1979)
0.038-0.38 (0.03-0.3)	Recommended TLV			X	Kane and Alarie (1977)
0.25 (0.2)	Recommended exposure limit		X		Hanrahan et al. (1980)
0.15 (0.12)	Recommended ceiling exposure limit in Denmark		X		NRC (1980) Andersen (1979)
0.12 (0.1)	Ceiling exposure limit recommended by the AIHA	X			NRC (1980)
0.12 (0.1)	Ceiling exposure limit promulgated in The Netherlands and recommended in West Germany		X		NRC (1980) Andersen (1979)
0.075 (0.06)	Standard for the maximum immission concentration (MIC) for short-term exposures in West Germany	X			Helwig (1977)
0.035	Standard for maximum one-time exposure in populated places in the USSR	X			USSR (1972)

(Continued)

TABLE VII-2 (concluded)

HCHO Level in mg/m³ (ppm)	Recommendation/Regulation	Type of Exposure			Reference
		Outdoor Air	Indoor Air	Occupational Air	
0.025 (0.02)	Standard for the MIC for long-term exposure in West Germany	X			Helwig (1977) NRC (1980)
0.025 (0.02)	Standard in The Netherlands for levels 2 mo after installation of urea-HCHO foam insulation		X		Rumack (1978)
0.012	Standard for maximum avg. exposure in populated places in the USSR	X			USSR (1972)
0.01 (0.008)	Promulgated ceiling exposure limit in the USSR	X			NRC (1980)
0.004 (0.003)	Recommended highest concentration for Air Quality Standard	X			Kane et al. (1979)

The upper limit of a range of concern for nonoccupationally exposed humans based on short-term experimental exposures should be 0.95-1.0 mg HCHO/m^3, where eye irritation is slight, the odor is perceived, and other effects occur (changes in breathing rhythm and α-rhythms). The lower level should be at least 0.2-0.25 mg/m^3, which is the threshold for eye irritation. Perhaps the lower level should be 0.05 mg/m^3, the lowest reported odor threshold.

From occupational, epidemiological, and similar public exposure reports, a level of concern of 0.211 mg HCHO/m^3 may be recommended. This concentration produced eye and upper respiratory tract irritation in moderately long-term exposures whereas no such symptoms were observed in adult or school children exposed to 0.08-0.13 mg/m^3.

Thus, the human studies indicate that the range of concern in long-term or acute exposures to HCHO should be 0.06 or 0.2 to ~ 1 mg/m^3. If animal studies were directly extrapolatable to humans, it would appear prudent to make the lower limit of the range of concern 0.01-0.04 mg/m^3.

The value of 0.2 mg/m^3 may be the most defensible choice since both nonsmoking and smoking humans sometimes contain aldehydes in the breath at levels as high as ~ 0.1 mg/m^3, HCHO being a normal metabolite and a metabolite of exogenous substances. This value is frequently the maximum value reported for urban polluted air. However, various authorities have recommended or promulgated standards for HCHO in outdoor air as low as 0.01 mg/m^3.

ANNOTATED BIBLIOGRAPHY

5-175* ACGIH, American Conference of Governmental Industrial Hygienists. 1971. Documentation of the Threshold Limit Values for Substances in Workroom Air. ACGIH, Cincinnati, Ohio. pp. 118-119.

C--.** ACGIH recommended a ceiling limit for HCHO in workplace air of 2 ppm; ANSI in 1967, 3; the USSR in 1966, 0.8; and Czechoslovakia in 1969, 1.6 ppm. The ACGIH limit was set to avoid upper respiratory tract irritation in most workers. A limit of 5 ppm would be low enough to prevent respiratory injury.

5-421 ACGIH, American Conference of Governmental Industrial Hygienists TLV Airborne Contaminants Committee. 1980. TLVs Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment with Intended Changes for 1980. ACGIH Cincinnati, Ohio. p. 19.

A--. The time-weighted-average TLV for HCHO is 3 mg/m^3 (2 ppm).

5-179 Ahmad, I., and T. Whitson. 1973. Formaldehyde: How Much of a Hazard? Ind. Med. Surg. 42(8):26-27.

C-4. Employees of an industrial garment company lost consciousness after short exposure to at least 2.5-12.5 mg $HCHO/m^3$. Continued headache, dizziness, nausea, and some tremors. Other employees seemed unaffected, when observed later in the day.

5-407 AIHA, American Industrial Hygiene Association. 1978. Hygiene Guide Series; Formaldehyde. American Industrial Hygiene Association, Akron, Ohio. 5 pp.

C--. Review.

5-218 Alabert, N., J. Godin, C. Boudene, and A. Roussel. 1971. The Effect of Aldehyde Atmospheric Pollutants on the NAD-NADH System of the Liver, Lungs, and Encephalon in Rats. C. R. Hebd. Seances Acad. Sci., Ser. D. 272(26):3363-3366 (Fre).

D-6. After 3-h exposure to 140 ppm HCHO, the rats were immediately sacrificed and the levels of NAD and NADH in the brain, liver, and lungs were determined. Only the level of NAD in the brain decreased significantly. Few details of the methodology are given. Other aldehydes were studied, leading to the suggestion that after passing the respiratory barrier, aldehydes may have a specific toxic action at the cellular level.

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* Numbers in the left margin are MRI document acquisition numbers.

** MRI rating. See full explanation in Chapter I.

5-219 Alarie, Y. 1973. Sensory Irritation by Airborne Chemicals. C.R.C. Crit. Rev. Toxicol. 2(3):299-363.

D--. Extensive review of respiratory tract sensory receptors, the reflux reactions evoked following their stimulation by inhaled chemicals, the nature of chemicals eliciting sensory irritation, and the mechanisms of their interactions with nerve endings. Concerned primarily with acute exposures. Concludes that measurements of decrease in respiration rate in animals is a reliable predictor that an airborne chemical will evoke sensory irritation in humans.

5-217 Akabane, J. 1970. Aldehydes and Related Compounds. Int. Encycl. Pharmacol. Ther. Sect. 20, Vol. II, pp. 544-560.

C--. A review of the metabolism, toxicity, and pharmacological effects of lower aliphatic aldehydes, especially formaldehyde and acetaldehyde. 190 literature references.

5-022 Altshuller, A. P. 1978. Assessment of the Contribution of Chemical Species to the Eye Irritation Potential of Photochemical Smog. J. Air Pollut. Control Assoc. 28(6):594-598.

D-8. A review and discussion of the results of several studies on atmospheric samples or irradiated auto exhaust and hydrocarbon-nitrogen oxide mixtures. The eye irritation on a moderately smoggy day may be due 40% to HCHO and 25% to acrolein. Atmospheric samples collected in California contained 30-66 ppb HCHO and 6-7 ppb acrolein.

5-001 Amdur, M. O. 1960. The Response of Guinea Pigs to Inhalation of Formaldehyde and Formic Acid Alone and With a Sodium Chloride Aerosol. Intern. J. Air Pollut. 3(4):201-220.

B-13. Guinea pigs were exposed to HCHO at 0.05-50 ppm alone and in combination with NaCl aerosol. Upper vs. lower respiratory effects are compared through use of normal and tracheotomized animals.

5-204 Amdur, M. O. 1966. The Respiratory Response of Guinea Pigs to Histamine Aerosol. Arch. Environ. Health 13(1):29-37.

D--. Study of guinea pigs' response to histamine aerosols compared to responses to HCHO determined earlier. Same HCHO data as in Amdur (1960).

5-024 Amdur, M. O. 1978. Respiratory Response to Iodine Vapor Alone and with Sodium Chloride Aerosol. J. Toxicol. Environ. Health 4(4):619-630.

D--. Study of guinea pig responses to I vapor and NaCl aerosol as compared to responses to HCHO determined earlier. Same HCHO data as in Amdur (1960).

5-310 Andersen, I. 1979. Formaldehyde in the Indoor Environment--Health Implications and the Setting of Standards. In: Indoor Climate, Effects on Human Comfort, Performance, and Health in Residential, Commercial, and Light-Industry Buildings., Proc. of the First Int. Indoor Climate Symp., Copenhagen, Denmark. August 30-September 1, 1978. P. O. Fanger and O. Valbjorn, Eds. Danish Building Research Institute, Copenhagen, Denmark. pp. 65-87.

A-14. Literature review with 16 references. Results of a human experimental study exposing 16 people to 0.3, 0.5, 1.0, and 2.0 mg HCHO/m^3 for 5 h each on consecutive days. No changes in airway resistance, small decrease in nasal mucus flow except at 1.0 mg/m^3, eye irritation and dryness in nose and throat at all levels, and no change in performance tests were reported. Suggest a standard for continuous exposure to HCHO of $\leq$ 0.15 mg/m^3. Panel discussion of the paper included the information that the Netherlands recommended and Germany published an indoor air standard of 0.12 mg/m^3.

5-205 Andersen, I., G. R. Lundqvist, and L. Molhave. 1975. Indoor Air Pollution Due to Chipboard Used as a Construction Material. Atmos. Environ. 9(12):1121-1127.

C--. HCHO concentrations in 25 rooms in 23 Danish homes using chipboard construction materials were 0.08-2.24 mg/m^3 (avg. 0.62 mg/m^3). The West German limit for outdoor ambient air (0.03 mg/m^3) was exceeded in all cases. (The West German workplace limit is 1.2 mg/m^3.)

5-025 Anderson, R., and Y. Alarie. 1978. Respiratory Toxicity of Theral Decomposition Products of Urea Formaldehyde and Phenol Formaldehyde. Pharmacologist 20(3):197.

D--. Abstract of work completely described in Anderson et al. (1979) [5-026].

5-026 Anderson, R. C., M. F. Stock, R. Sawin, and Y. Alarie. 1979. Toxicity of Thermal Decomposition Products of Urea Formaldehyde and Phenol Formaldehyde Foams. Toxicol. Appl. Pharmacol. 51(1):9-17.

D-7. Mice were exposed to thermal decomposition products of urea- and phenol-formaldehyde foams. Study too confounded to be useful. Authors stated HCHO was not the cause of acute mortality from either foam.

5-027 Anonymous (Editorial). 1979. Formaldehyde Toxicity. Lancet 2(8143):620-621.

C--. This editorial cites only a few references on the inhalation toxicity of HCHO, yet one of its citations was one we were not aware of. (Ozhiganova et al., 1977 [5-377]). Three mechanisms are enumerated by which HCHO vapors may cause chest disease: immunological reaction, direct histamine release from mast cells, and stimulation of bronchial irritant receptors.

5-415 Anonymous. 1980a. Dr. Selikoff Expresses Reservations about Formaldehyde Study. Occup. Health Safety Lett. 10(11):2.

D--. The reservations were: no verification of the contention that plants producing HCHO or HCHO-based resins are the most promising resources for cohort mortality studies; voluntary participation of workers and companies would introduce selection bias; confidentiality of the data; the need for an "exemplary professional input," a full-time epidemiologist; and the possible problem of a cohort of insufficent size and duration from onset for meaningful results.

5-416 Anonymous. 1980b. Westat Awarded Data Collection Contract for Formaldehyde Study. Occup. Health Safety Lett. 10(12):2-3.

D--. A response to some of Dr. Selikoff's reservations (Anonymous, 1980a).

5-422 Anonymous. 1980c. Clinical Approach to Quantitating Formaldehyde Effects in Human Blood. In: Workshop on Indoor Air Quality Research Needs. Interagency Research Group on Indoor Air Quality. Washington, D.C. p. H-15.

D--. Very brief description of a project attempting to correlate blood levels of HCHO with changes in human chromasomal material in cultured human lymphocytes.

5-401 Anonymous. 1981a. Formaldehyde, Cadmium Highlighted in Toxicology Forum Sessions. Pest. Toxic Chem. News 9(21):12-13.

C--. Article summarizes the 24-mo results of the CIIT-sponsored study in rats and mice that found a high incidence of nasal carcinomas in rats exposed to 15 ppm HCHO.

5-414 Anonymous. 1981b. Support Services for a Mortality Study of Workers Exposed to Formaldehyde. Commerce Bus. Dly. April 17. p. 1.

D--. Announcement of a request-for-proposal, the study sponsored by the Formaldehyde Institute and the National Cancer Institute.

-- Anonymous. 1981c. Formaldehyde Institute Disputes NYU's Dr. Upton in Letter to OSHA. Occup. Health Safety Lett. 11(17)[September 8]:1-2.

C--. Includes a brief description of study by NYU, finding "grossly" visible nasal tumors in 10% of rats exposed to 14 ppm HCHO for 382 6-h periods. Formaldehyde Institute contends that the animal data are inconclusive, that what data there are suggest a possible threshold for carcinogenicity, and that human data are negative.

-- Anonymous. 1981d. Study shows Formaldehyde is Carcinogenic. Science 213(11):1232.

C--. Includes a brief mention of a study by NYU, finding nasal cancers in 10% of rats exposed to 10.6 and 14.6 ppm HCHO.

6-116 Apol, A. G., 1973. Health Hazard Evaluation/Toxicity Determination Report 72-32-42; Union Pacific Railroad, Pocatello, Idaho. PB 229 161, National Technical Information Service, U.S. Department of Commerce, Springfield, VA. 23 pp.

D--. 117 workers were exposed to acrolein (0.014-0.04 ppm), HCHO (0.015-0.07 ppm), CO (< 1-15 ppm), NO_x (0.03-0.26 ppm), SO_2 (< 0.01 ppm), and particulates (0.09-0.26 mg/m^3). No excess of chronic respiratory disease. Eye irritation and headaches reported.

5-221 Apol, A. G. 1976. Health Hazard Evaluation Determination Report Number 76-38-326, Rycraft, Inc., Corvallis, Oregon. PB-273748, National Technical Information Service, U.S. Department of Commerce, Springfield, VA. 11 pp.

D--. Although the metals Co, Pb, Mn, Sn, and V and phenols were not detected in the workplace samples, the employees suffered slight nose and throat irritation ("expected responses at the concentrations found and are not considered detrimental") from exposure to ≦ 0.16 ppm HCHO and ≦ 0.4 ppm SO_2.

5-002 Auerbach, C., M. Moutschen-Dahmen, and J. Moutschen. 1977. Genetic and Cyto-genetical Effect of Formaldehyde and Related Compounds. Mutat. Res. 39:317-362.

D--. Review. Pages 326-343 deal with the effects of a "formaldehyde food" - a Drosophila melanogaster diet of unknown composition containing sublethal levels of formalin. The authors reviews the speculations of other authors using this mixture as to the biochemical mechanisms of effects seen in the test animals (fruit flies). Respiratory exposures and effects on mammals are not discussed.

5-029 Avdeeva, I. A., V. P. Agudin, L. M. Barysheva, B. I. Karpunin, and I. Ya. Saidasheva. 1980. Physiological-Hygienic Evaluation of the Work of Women in Plywood Production. No. 2:30-32 (Russ).

D-4. Workers exposed to ~ 1.5-2.5 mg HCHO/m^3 and wood dust at 1.5-2x the MAC, and had $\geq$ 5 y service. Complained of muscle fatigue in the hands and feet, general weakness, headache, and eye fatigue. The highest morbidity was due to colds and flu. Women had higher frequency of loss of work capacity and cardiovascular illness. The results of this uncontrolled study probably reflect the nature of the work (heavy labor) more than the HCHO exposure.

5-329 Barnes, E. C., and H. W. Speicher. 1942. The Determination of Formaldehyde in Air. J. Ind. Hyg. 24:10-17.

C-3. Primarily a discussion of the methods for taking HCHO measurements, and their efficiencies. Exposure to 20 ppm HCHO while testing caused immediate and strong eye, nose, and throat irritation. Workers in industrial areas sampled didn't seem to object to HCHO levels < 5 ppm.

5-322 Basmadzhieva, K., T. Burkova, M. Argirova, St. Milanov, and E. Davidkova. 1974. Biological Effect of Threshold Concentrations of Hydrochloric Acid and Formaldehyde Inhaled into the Organism. Khig. Zdraveopaz. 17(5):480-486 (Bulg).

B-9. Chronic exposure of rats to 0.035 mg/m^3 of HCHO resulted in 20-30% decrease in bioenergetic metabolism processes in mitochondrial fraction of liver from 1st mo through 6 mo exposure.

5-336 Batulin, Yu M., A. L. Klyashchitskaya, and N. K. Kulagina. 1972. Toxicology of an FM-1322 Organosilicon Heat-Transfer Agent. Gig. Tr. Prof. Zabol. 16(3):56-58 (Russ).

D-9. Female rats exposed to the gases evolved from the heating of poly(methylphenylsiloxane) ($\leqq$ 20 mg CO/m^3, $\leqq$ 0.635 mg HCHO/m^3, 0.005 vol. % CO_2, and $\leqq$ 20 mg C_6H_6/m^3) did not show any significant differences from the controls with respect to the summation threshold, O_2 consumption, morphological condition of the blood, and growth dynamics.

5-031 Baur, X., and G. Fruhmann. 1979. Bronchial Asthma of Allergic or Irritative Origin as an Occupational Disease. Prax. Klin. Pneumol. 33(Suppl. 1):317-322 (Ger).

C-8. A 47-y-old female chemical plant worker complained of eye watering, head cold, coughing, and asthma when exposed to formalin vapors (no concentrations given). There was a slight decrease of IgG (0.8 g/L) and a negative reaction to skin tests with formalin and the usual inhalation allergens. A 5-min provocation inhalation test with vapors from a 25% formalin solution produced severe bronchoconstriction, running nose, and watering eyes. Dry cough appeared 3-5 h later. After being away from work for 2 wk, the responses required a 25-min exposure and a slight bronchial reaction occurred after 5 h.

6-005 Beckner, J.S., P. M. Hudgins, and J. L. Egle, Jr. 1974. Effects of Acetaldehyde, Propionaldehyde, Formaldehyde, and Acrolein on Contractility, Carbon-14-Labelled Norepinephrine and Calcium-45 Binding in Isolated Smooth Muscles. Res. Commun. Chem. Pathol. Pharmacol. 9(3):471-488.

D-16. Good, well-done pharmacology. Mechanisms of structural congeners on isolated rat vas deferens and rabbit aorta (smooth muscle). Does not help define inhalation exposure levels. 10^{-2} M HCHO and 10^{-3} M acrolein gave similar responses.

5-032 Berk, J. V., C. D. Hollowell, and C. I. Lin. 1979. Indoor Air Quality Measurements in Energy-Efficient Houses. LBL-8894, National Technical Information Service, U.S. Dept. of Commerce, Springfield, VA. 27 pp.

C--. An Energy Research House in Ames, Iowa, contained 28-61 ppb HCHO (avg. 42 ppb) in the indoor air compared to < 7 ppb outdoors.

5-427 Blackwell, M., H. Kang, A. Thomas, and P. Infante. 1981. Formaldehyde: Evidence of Carcinogenicity. Am. Ind. Hyg. Assoc. J. 42(7):A34, A36, A38, A40, A42, A44, A46; NIOSH Current Intelligence Bulletin #34.

C--. Review. NIOSH recommends that HCHO be handled as a potential occupational carcinogen. Doesn't necessarily represent the official evaluation of OSHA.

5-123 Blejer, H. P., and B. H. Miller. 1966. Occupational Health Report of Formaldehyde Concentrations and Effects on Workers at the Bayly Manufacturing Company, Visalia, California. Study Report No. S-1806 of California Health and Welfare Agency, Dept. of Public Health, Bureau of Occupational Health, Los Angeles, California. 6 pp.

C-3. The manufacture of permanently pressed pants released HCHO into the workplace atmosphere, causing levels of 1.1-3.4 mg/m^3. Eye, nose, and throat irritation was intense for ~ 20 min, then some apparent habituation occurred. Wasn't considered a systemic health hazard.

5-003 Bokina, A., and N. Eksler. 1973. Electrophysiological Analysis of the Action of Certain Atmospheric Pollutants [illegible] the Central Nervous System. Gig. Sanit. No. 12. 11-16 (Russ).

B-7. EEG's of rabbits exposed to HCHO in concentrations from 0.035 to 6.5 mg/m^3 for 10 s to 1.5 mo showed detrimental effects except for the lowest level used for 20 min. Stress such as noise or flashing light accompanied some of the exposures.

5-222 Bokina, A. I., N. D. Eksler, A. D. Semenenko, and R. V.Merkur'yeva. 1976. Investigation of the Mechanisms of Action of Atmospheric Pollutants on the Central Nervous System and Comparative Evaluation of Methods of Study. Environ. Health Perspect. 13:37-42.

B-2. There is little experimental detail on HCHO in this English-language article, but it does give some of the results of the studies by Bokina and Eksler (1973) [5-003] and Fel'dman and Eksler (1975) [5-184] and helps in the translation of the Russian terms used. The overall electrical activity of various brain structures of rabbits was studied in response to O_3, HCHO, and CS_2. The brain structures that account for the sensory response to olfactory stimuli are the olfactory bulb and piriform complex [the amygdaloid nucleus ?]. Those that organize adaptive-behavioral reactions are the hippocampus, amygdala, and reticular formation of the brain stem.

5-224 Bonashevskaya, T. I. 1973. Amygdaloid Lesions after Exposure to Formaldehyde. Arkh. Anat., Gistol. Embriol. 65(12):56-59 (Russ).

B-8. Rats exposed for 3 mo to 3 mg HCHO/m^3 showed definite structural and cytological shifts in their amygdaloid complexes compared to those of the controls. Changes in the relation of the chronaxy of the muscles-antagonists were seen by the 2nd wk and 2nd mo in rats exposed to 3 and 1 mg HCHO/m^3, respectively. Cholinesterase activity was lowered significantly in rats exposed to 3 but not to 1, 0.035, or 0.012 mg HCHO/m^3.

5-223 Bonashevskaya, T. I. 1975. Barrier Function of the Nasal Mucosa During Action of Atmospheric Pollutions. Gig. Sanit. No. 9:14-17 (Russ).

C-5. Rats exposed to 0.12 mg HCHO/m^3 for 3 mo showed morphological degenerative and proliferative changes in the nasal mucosa not seen with 0.012 mg HCHO/m^3 (the ambient air MAC). However, the same changes were ascribed to benzene, toluene, xylene, m- and p-chlorophenyl isocyanate, chlorophos, hexane, and pentane also at 10 X their ambient air MAC's but not at the MAC levels.

5-126 Bourne, H. G., and S. Seferian. 1959. Formaldehyde in Wrinkle-Proof Apparel Produces--Tears for Milady. Ind. Med. Surg. 28: 232-233.

C-3. Uncombined HCHO from the treatment process is emitted, resulting in levels in dress stores of 0.16-0.56 mg HCHO/m^3. Customers and employees complained of strong odor and eye and throat irritation.

5-311 Breysse, P. A. ed. 1977. Formaldehyde in Mobile and Conventional Homes. Environ. Health Saf. News 25(1-6): 20 pp.

B-6. A review of HCHO toxicity, case reports of some HCHO exposure incidents, and the early results of a mobile and conventional homes study for HCHO exposure. More extensive results are discussed in Breysse (1978) [5-357], Breysse (1979a) [5-355], Breysse (1979b) [5-356], and Breysse (1980b) [5-354].

5-357 Breysse, P. A. 1978. Formaldehyde Exposure Following Urea Formaldehyde Insulation. Environ. Health Saf. News. 26(1-12): 13 pp.

B-6. Several case reports, and the results of a study of HCHO exposure. In 39 conventional homes with UF insulation, HCHO levels ranged from 0.05 to 3.40 ppm, with 80% of the samples < 0.5 ppm. Eye, nose, and respiratory tract irritation and headaches were the most frequent complaints.

5-355 Breysse, P. A. 1979a. Formaldehyde Exposure in Mobile Homes and Conventional Homes. In: Proc. 43rd Ann. Educational Conference of the National Environmental Health Association, June 23-28, 1979. 16 pp.

B-6. A less detailed discussion of the same study described in Breysse (1978) [5-357], Breysse (1977) [5-311], Breysse (1979b) [5-356], and Breysse (1980b) [5-354].

5-356 Breysse, P. A. 1979b. Formaldehyde Exposure In Mobile Homes. In: Proc. 39th Ann. AMA Congress on Occupational Health, University of North Carolina, October, 1979. 17 pp.

B-7. The same report as Breysse (1980b) [5-354], and a continuation of the study described in more detail (although of fewer homes) in Breysse (1977) [5-311].

5-354 Breysse, P. A. 1980b. Small Plants and Their Medical Problems--The Furniture Industry. The Environmental Problems of Urea-Formaldehyde Structures--Formaldehyde Exposure In Mobile Homes. In: Occupational Safety and Health Symposia, 1979. Publication No. (NIOSH) 80-139. U.S. Dept. of Health and Human Services, Cincinnati, Ohio. pp. 56-64.

B-7. The same report as Breysse (1979b) [5-356]. Residents of 334 mobile homes were exposed to HCHO levels from 0.04 to 2.21 mg/m^3, with 66% between 0.13 and 0.61 mg/m^3. Irritation of the eyes, nose, and throat were the primary symptoms. Differences between adults and children were considered. No control or comparison group.

5-425 Brooks, S. M., and C. F. Reinhart. 1981. Health Effects of Formaldehyde. In: Formaldehyde and Other Aldehydes. Committee on Aldehydes, National Research Council. National Academy Press. Washington, D.C. pp. 175-220.

C--. This authoritative review of the health effects of HCHO is organized by type of toxic effect rather than by route and dose.

5-128 Brunnthaler, J. 1913. The Toxic Effects of Formaldehyde. Aerztl. Sachverstaendigen-Zeitung. 19(7):142-146 (Ger).

C--. A good review of early reports on the toxic effects of oral and inhalation exposures to formaldehyde.

5-035 Burdach, S., and K. Wechselberg. 1980. Damages to Health in Schools. Complaints Caused by the Use of Formaldehyde-Emitting Materials in School Buildings. Fortsch. Med. 98(11):379-384 (Ger).

B-9. Teachers and pupils in school buildings with atmospheric levels of 0.1-1.21 mg HCHO/m^3 complained of mucous membrane irritation and loss of concentration. Fewer symptoms were reported 8 mo after the removal of the HCHO-emitting chipboard.

5-374 Burian, K. 1960. Histological Changes in the Nasal Mucosa After Formalin Adaptation and Increased Crossed Resistance. Acta Otolaryngol. 52:429-437 (Ger).

D--. Rats were exposed 1 h/d for ≤ 7 wk to vapors from 2.5, 3.75, or 5% formalin solutions. The HCHO concentration in the air was not measured. Metaplastic epithelial cells were observed after healing of the initial epithelial damage.

5-225 Cali, G. 1965. Modifications Induced by Irritating Vapors on Mast Cells of Nasal Mucosa of the Rat. Clin. Otorinolaringoiatr. 17(2):117-128 (Ital).

D-5. Study of the effect of exposure of rats to 20% HCHO vapors for 3-5 min/d for 2-20 exposures. Damage to epithelium and the inflammation of nasal passages, more pronounced in rats exposed 10-20 times, but not present in rats restrained from rubbing their noses. In rats with only 2 exposures, mast cells of nasal mucosa were modified by increase in number, greater variety in shapes, increased tint affinity, and pronounced degranulation tendency. In rats exposed 10-20 times, same types of changes were reported, but less pronounced, particularly those concerning the degranulation phenomena.

5-129 Carpenter, C. P., H. F. Smyth, and U. C. Pozzani. 1949. The Assay of Acute Vapor Toxicity and the Grading and Interpretation of Results on 96 Chemical Compounds. J. Ind. Hyg. Toxicol. 31:343-346.

D-5. Study to develop a toxicity screening method. HCHO at 250 ppm or 8 ppm acrolein killed 2-4 of 6 albino rats exposed for 4 h.

6-118 Carson, S., R. Goldhamer, and M. S. Weinberg. 1966. Characterization of Physical, Chemical, and Biological Properties of Mucus in the Intact Animal. Ann. N.Y. Acad. Sci. 130:935-943.

D--. Primarily a discussion of the effects of cigarette smoke. Brief mention of HCHO as an irritant. Acrolein was the most effective in reducing mucus flow rates in cats after short-term inhalation exposures.

5-378 Chaigneau, M. 1980. Classification of Harmful Gases. Ann. Anesthesiol. Fr. 21(6):683-688 (Fre.).

D--. Very brief reviews (with no references) of the toxicity of several gases, including HCHO. Acrolein is mentioned as being lethal in ≤ 10 min at 30-100 ppm.

5-038 Chanet, R., and R. C. Von Borstel. 1979. Genetic Effects of Formaldehyde in Yeast. 3. Nuclear and Cytoplasmic Mutagenic Effects. Mutat. Res. 62:239-253.

C-10. In yeast cells, Saccaromyces cerevisiae, HCHO was a weak mutagen. (Much detail about strain/allele specificities/repair processes that is probably relevant to genetic researchers but not our task).

5-037 Chanet, R., C. Izard, and E. Moustacchi. 1976. Genetic Effects of Formaldehyde in Yeast. II. Influence of Ploidy and of Mutations Affecting Radiosensitivity on its Lethal Effect. Mutat. Res. 35:29-38.

C-12. Important in that this assay demonstrates that the HCHO-induced single strand DNA breaks appear to be repaired. This has ramifications in overall long-term effects if these principles apply to mammalian systems.

7-008 Chernomorskii, A. R., L. N. Zimont, R. A. Druz, L. N. Sigalova, E. F. Drigo, and G. G. Antipova. 1978. Study of Respiratory System Function in Workers Involved in a New Casting Process Using Cold-Hardening Molding Sands (based on the Resin BS-40). Gig. Tr. Prof. Zabol. No. 5:47-49 (Russ).

D-9. Workers were exposed to 2 mg HCHO/m^3, dust at 10x the MAC, phenol, aldehydes, methanol, cyanides, and CO (the last 5 at < MAC's) for up to 3 y. Respiratory pathology and functional changes were reported. Teplyakov et al. (1980) reported on apparently same group (1976 results), giving slightly lower HCHO levels (0.1-1.2 mg/m^3). They concluded that exposure had not caused expressed pathological changes.

5-226 Chizhikov, V. A. 1970. On the Use of Animals with a Simulated Disease in Studies of Hygienic Standards. Hyg. Sanit. 35(5): 182-186.

C-6. Exposure of hormonally deficient (castrated) male rats to 0.9 to 5 mg/L HCHO for 4 h. Test animals exhibited considerably less resistance, their mortality was higher, and survival time shorter than in controls.

5-428 Clary, J. J. 1980. A Review of the Health Effects of Formaldehyde. In: Proc. 14th Wash. State Univ. Int. Symp. Particleboard. pp. 125-136.

B--. A review of animal and human data, pointing out problems in protocol and interpretation. Argues that rats are not a good model for human cancer, and that the carcinogenicity found in the CIIT study may have been due to the severe irritation and tissue damage, and that there is a threshold for this, and thus for possible carcinogenicity. Includes a brief presentation of a study conducted by the Formaldehyde Institute, in which monkeys, rats, and hamsters were exposed to 0.2, 1, or 3 ppm HCHO for 6 mo. No adverse effects were found at the lowest levels; slight effects, at 3 ppm.

5-419 Cleveland, W. W., T. E. Graedel, and B. Kleiner. 1977. Urban Formaldehyde: Observed Correlation with Source Emissions and Photochemistry. Atmos. Environ. 11:357-360.

C--. HCHO levels were measured during the summer months of 1972, 1973, and 1974 in four different New Jersey cities: Bayonne, 3-12 ppb; Newark, 4-14 ppb; Camden, avg. 3.8 ppb; and Elizabeth, avg. 5.5 ppb. Levels varied during the day and the week with amount of automobile traffic and photochemical formation.

5-319 Comber, R., and P. Grasso. 1973. The Effects of Chemical Irritants and Tobacco Smoke Condensate on the Chorioallantoic Membrane of the Fertile Hen's Egg. Chem.-Biol. Interactions. 6:25-34.

C--. Development of a test system. HCHO (0.625-10 μg/μl) was applied to the chorioallantoic membrane of fertile hen's eggs. After 72 h, a dose-related hyperplasia (increased thickening of the membrane) was observed. Hyperplasia may be a necessary step in tumor promotion.

5-359 CPSC, Consumer Product Safety Commission. 1978. Summary of In-Depth Investigations: Urea-Formaldehyde Foam Home Insulation. Directorate for Communication, U.S. Consumer Product Safety Commission, Washington, D.C. 15 pp.

B-2. Brief summaries of 118 complaints and studies of adverse health effects following the installation of urea-formaldehyde foam insulation. HCHO levels ranged from < 0.5 to 7.0 ppm. Symptoms were primarily headache, eye and upper respiratory tract irritation, and nausea.

5-116 CPSC, Consumer Product Safety Commission. 1980a. Evaluation of Health Risks of Formaldehyde by Government Scientists. Fed. Regist. 45 (100):34031-34033.

C--. This is the announcement of the formation of the Formaldehyde Panel and the questions to be addressed by their November 1980 report, which see: Griesemer et al. (1980). The bibliography was consulted for additional references.

5-309 CPSC, Consumer Product Safety Commission. 1980b. Urea-Formaldehyde Foam Insulation; Proposed Notice to Purchasers. Fed. Regist. 45(113):39434-39444.

C--. The proposed written notice to prospective purchasers and first purchasers of insulation products made of urea-formaldehyde foam is to include the following statements: "This product may release formaldehyde gas into your home over a long period of time. Formaldehyde gas may cause eye, nose, and throat irritation, coughing, shortness of breath, skin irritation, nausea, headaches and dizziness. People with respiratory problems or allergies may suffer more serious reactions, especially persons allergic to formaldehyde." This publication summarizes actions by state and local governments and other federal agencies concerning urea-HCHO foam insulation. It describes the agency's investigation of consumer complaints and among symptoms of chronic impairment includes "loss of visual acuity." Numerous medical and scientific literature references cited were acquired for this task.

5-420 CPSC, Consumer Product Safety Commission. 1981. Urea-Formaldehyde Foam Insulation; Proposed Ban. Fed. Regist. 46(24):11888-11211.

C--. The discusion supporting the proposal reviews the report of the Formaldehyde Panel, the CIIT rat and mice studies showing nasal cancers, and numerous other primary literature reports. The Commission staff estimated that "any person living in a U.S. foam insulation home for seven years after the product is installed would have, as an upper estimate, an 85 in a million additional risk of developing cancer from the formaldehyde released by the insulation. The Commission has concluded "Based on the report of the Federal Panel as well as additional research by Mantel and Schneiderman, the risks to laboratory rats of developing cancer should be considered to apply directly to humans breathing the same concentration of formaldehyde (in ppm) as the test animals." The Commission had requested the National Academy of Sciences (NAS) to determine whether there is a tolerable level of HCHO in residential indoor air. The NAS committee of expert toxicologists concluded that "there is no population threshold for the acute irritant effects of formaldehyde in humans."

5-176 Coon, R. A., R. A. Jones, L. J. Jenkins, Jr., and J. Siegel. 1970. Animal Inhalation Studies on Ammonia, Ethylene Glycol, Formaldehyde, Dimethylamine, and Ethanol. Toxicol. Appl. Pharmacol. 16(3): 646-655.

B-12. Chronic exposure of 5 animal species to 4.6 mg HCHO/m^3 for 90 d produced one rat death and inflammatory changes in lungs, heart, and kidneys.

5-365 Cooper, P. 1979. Genetic Effects of Formaldehyde. Food Cosmet. Toxicol. 17:300-301.

C--. A review with selective points of view presented from several authors. These include: (1) action of HCHO on bacterial DNA is through products of reaction of HCHO with amino-containing compounds or the free amino acids present in the bacterial cells, not directly by HCHO; (2) radiation and HCHO appear to share a common step in damage/repair of the breaks which occur in Saccharomyces cerevisiae (yeast) pyrimidine dimers.

5-333 Cralley, L. V. 1942. The Effect of Irritant Gases Upon the Rate of Ciliary Activity. J. Ind. Hyg. Toxicol. 24:193-198.

C-10. Exposure of rabbit tracheal preparations to 30-60 ppm HCHO for 10 min or 60-100 ppm for 5 min caused cessation of ciliary activity without recovery in Ringer's solution. Exposure to 18-20 ppm for 10 min or 30 ppm for 5 min caused cessation of activity without recovery in air.

5-220 Criteria for Community Air Quality Committee. 1968. Community Air Quality Guides. Aldehydes. Am. Ind. Hyg. Assoc. J. 29(5): 505-512.

C--. The toxicology and ambient concentrations of specific aldehydes including HCHO and acrolein are reviewed. In automobile exhaust, ~ 70 mol-% of the carbonyl compounds, which are mainly aldehydes, is HCHO. Acrolein and acetaldehyde comprise 3-10 mol-%. Avg. U.S. urban air concentrations are 0.06 ppm HCHO (~ 0.09 mg/m^3) and 0.006 ppm acrolein (~ 0.015 mg/m^3). Recommended levels (causing no sensory irritation) are 0.1 ppm HCHO, 0.01 ppm acrolein, and 0.2 ppm total aldehyde as HCHO.

5-429 Dalbey, W. E. 1981. Effects of Formaldehyde or Nitrogen Dioxide on Tumors in Hamster Respiratory Trace. Submitted to Toxicology for publication; draft copy sent to Midwest Research Institute by author.

B-12. Exposure of hamsters to 10 ppm HCHO five times/wk for lifetime caused no tumors or adverse effects on nasal epithelium.

Concurrent exposure of 30 ppm HCHO and subcutaneous injuections of diethylnitrosamine (DEN) increased the number of tumors per tumor-bearing animal above that of DEN alone.

3-027 Dalhamn, T. 1956. Mucous Flow and Ciliary Activity in the Trachea of Healthy Rats and Rats Exposed to Respiratory Irritant Gases (SO_2, H_3N, HCHO). VIII. The Reaction of the Tracheal Ciliary Activity to Single Exposure to Respiratory Irritant Gases and Studies of the pH. Acta Physiol. Scand. 36(Suppl. 123):93-105.

C-6. Tracheal ciliary movement was observed in rats apparently opened and exposed in situ to 0.5, 3, 10, or 22 ppm HCHO. Movement was stopped in 2.5 min and 10 s for the lowest and highest exposures, respectively. Recovery occurred in 30 s after the lowest exposure stopped.

5-228 Dalhamn, T., and A. Rosengren. 1971. Effect of Different Aldehydes on Tracheal Mucosa. Arch. Otolaryngol. 93(5):496-500.

C-5. A study of rabbit tracheal tissue showed that formaldehyde appeared to be the most ciliotoxic, followed by acetaldehyde and acrolein. Their experiments largely confirmed the results of other authors. Data for HCHO indicated that ciliotoxicity increased rapidly for small increases in the concentration of vapor, 61.7 mg/m^3 causing immediate cessation of ciliary activity.

5-229 Danilin, V. A., and V. P. Meshcheriakov. 1968. On the Aspects of Acute Formaldehyde and Dimethyldioxane Poisoning. Gig. Tr. Prof. Zabol. 12(7):45-46 (Russ).

D-3. The course of acute HCHO poisoning in workers is described, but no HCHO concentrations are given. Exposure is confounded by the presence of dimethyldioxane. Respiratory and skin symptoms disappeared in 2-3 d if there was no further contact with HCHO.

5-044 Davidkova, E., and E. Basmadzhieva. 1979. Changes in Protein and Nucleic Acid Metabolism as a Method for Assessing Gonadotoxic Effects. Probl. Khig. 4:101-109 (Bul).

B-7. Chronic exposure of male rats to 0.035 mg $HCHO/m^3$ decreased RNA content, deoxyribonuclease activity, and protein content in testicular homogenate. DNA content was increased. Sperm mobility was decreased.

5-230 Davis, T. R. A., S. P. Battista, and C. J. Kensler. 1965. Effect of Cigarette Smoke, Acrolein and Formaldehyde on Pulmonary Function. Fed. Proc. 24(2, Part I):518.

C-5. Exposure of both tracheotomized and intact guinea pigs with effect on lung function only in intact animals.

5-131 Davis, T. R. A., S. P. Battista, and C. Kensler. 1967. Mechanism of Respiratory Effects During Exposure of Guinea Pigs to Irritants. Arch. Environ. Health 15:412-419.

C-6. Exposure of guinea pigs to HCHO and acrolein using both tracheotomized and intact animals. Effect on lung function only in intact animals.

5-302 Deimel, M. 1978. Experience on the Formaldehyde Concentrations in Room Air of a New School Building. In: Urg. Verunreinig. Umwelt: Erkennen, Bewerten, Vermidern, [Tag.]. K. Aurand, U. Haesselbarth, E. Lahmann, G. Muller, and W. Niemitz, Eds. Erich Schmidt Verlag, Berlin, Germany. pp. 416-427 (Ger).

C--. The ambient air of new school buildings contained < 0.01 to 1.90 ppm HCHO with concentrations ≥ 0.31 ppm in the hot summer months.

5-231 Diamant-Berger, O. 1970. Forensic Evaluation of the Sequelae of Toxic Pulmonary Aggressions. Poumon Coeur 26(9):1013-1016 (Fre).

D-6. Case histories of exposures to several different gases, only two for HCHO. In one case an existing asthmatic condition was aggravated. In the other, a one-time asthma-like attack occurred, with no sequelae. Following a second exposure 3 y later, a characteristic, long-term asthma evolved. No HCHO levels or exposure times given.

5-045 Dost, F. N. 1979. Assessment of Potential Toxic Hazards of Formaldehyde. Proc. Wash. State Univ. Symp. Particleboard 13:317-327.

C--. A good review of the health effects of HCHO by a toxicologist.

5-341 Drobysheva, R. A., Y. V. Mitin, and A. M. Eskin. 1972. Experimental Study of the Combined Effect of Dimethyldioxane and Formaldehyde on the Air Passages. Gig. Tr. Prof. Zabol. 16(6):52-53 (Russ).

D--. Rats (20 per group) were exposed to a mixture of dimethyldioxane and HCHO in the concentrations 360 mg/m^3 plus 23 mg/m^3 or 544 mg/m^3 plus 29.7 mg/m^3, respectively, for 2 h/d, 5 d/wk for 9 wk. These values were ~ 36-60x the MAC's. Destructive changes were observed in the upper respiratory tract mucosa.

5-232 Dubreuil, A., G. Bouley, J. Godin, and C. Boudene. 1976. Continuous Inhalation of Low Levels of Formaldehyde: Experimental Study in Rats. Eur. J. Toxicol. Environ. Hyg. 9(4):245-250 (Fre); English translation available from John Crerar Library, Chicago, Illinois. Order No. 79-12804-06T.

B-10. Chronic exposure of rats to 3 levels of HCHO. No effect from ~ 2 to 5.7 mg/m^3, respiratory effects seen at ~ 10 mg/m^3 level.

5-234 Dubrovskaya, F. I., V. P. Levkin, and L. L. Zabudnyak. 1976a. Effect of Low Concentrations of Formaldehyde in a Chronic Inhalation Experiment. Gig. Aspekty Okhr. Okruzhayushchei Sredy. pp. 115-122 (Russ).

B-8. Exposing rats for 98 d to 0.012 or 0.031 mg HCHO/m^3 caused a fine focal pneumonia in the lungs, heart changes such as an increase of rhythm frequency and a decrease of electrical activity, and lowering of the function of the nerve cells of the brain.

5-233 Dubrovskaya, F. I., M. S. Katsenelenbaum, Y. K. Yushko, S. A. Ipatova, and P. P. Vlasov. 1976b. Hygienic Evaluation of Air Protection Measures at the Volga Industrial Complex. Gig. Aspekty Okhr. Ozkruzhayushchei Sredy. pp. 123-127 (Russ).

D--. Exposure of children living in the vicinity of the Volga industrial complex to HCHO, SO_2, aldehydes, H_2S, and NH_3 led to increased morbidity. Effects were not ascribed to particular substances and levels of the compounds were not stated except that they exceeded their limits.

5-171 Efremov, G. G. 1970. State of the Upper Respiratory Tract in Formaldehyde Production Workers. (Data of a Special Study). Zh. Ushn. Nos. Gorl. Bolez 30(5):11-15 (Russ).

A-10. Diseases of the upper respiratory tract were at least twice as prevalent in 278 workers of 2 wood-processing plants using urea-HCHO resins as in 200 age-matched, unexposed controls. Besides observable pathology, the nasal membranes showed functional disturbances as judged from the motility of the cilia, the absorptive capacity, and odor threshold measurements. Workers apparently became inured to the hazard with increasing length of service. Griesemer et al. (1980) [5-361], p. 43, concluded that if the controls were appropriate, the report supports the hypothesis that HCHO exposure may lead to chronic respiratory disease.

5-005 Egle, J. L. 1972. Retention of Inhaled Formaldehyde, Propionaldehyde, and Acrolein in the Dog. Arch. Environ. Health 25:119-124.

D-9. Anesthetized dogs were exposed to 0.15 to 0.35 μg/mL of HCHO or 0.4 to 0.6 μg/mL acrolein. Retention of HCHO in the total respiratory tract was nearly 100%, upper tract retention alone exceeded 95%. Retention of acrolein in the total respiratory tract was 81 to 84%, upper tract retention was 75 to 80%. Variations in concentration, ventilatory rate, or tidal volume had little effect on retention of the chemicals.

5-183 Egle, J. L., and P. M. Hudgins. 1974. Dose Dependent Sympathomimetic and Cardioinhibitory Effect of Acrolein and Formaldehyde in the Anesthetized Rat. Toxicol. Appl. Pharmacol. 28:358-366.

D-6. Primarily a study of i.v. exposure. Anesthetized rats were exposed by inhalation for 1 min to 0.01 to 5.00 μg acrolein/mL. As concentration increased a pressor effect of increasing magnitude was observed. Cardioinhibitory effect occurred at 2.50 and 5.00 μg/mL. HCHO concentrations up to 2.0 μg/mL did not produce any significant cardiovascular effects.

5-301 Einbrodt, H. J., and D. Prajsnar. 1978. Effect of Formaldehyde Exposure in School and Living Areas on People. In: Org. Verunreinig. Umwelt: Erkennen, Bewerten, Vermidern [Tag.]. K. Aurand, U. Haesselbarth, and E. Lahmann, Eds. Erich Schmidt Verlag, Berlin, Germany. pp. 428-435 (Ger).

B-6. Studies of 2 groups exposed to HCHO: school children (0.08-0.13 mg HCHO/m^3) and adults (0.25-0.75 mg HCHO/m^3). Complaints were reported only by adults exposed to the highest levels. By measuring HCHO and HCOOH levels in the urine, the authors conclude that exposure to $\leqq \sim 0.01$ mg HCHO/m^3 cannot be traced biologically. They recommend that the threshold value for schools and living areas should be between 0.1 and 0.5 ppm to avoid annoyance due to HCHO.

5-006 Einbrodt, H. J., D. Prajsnar, and J. Erpenbeck. 1976. The Formaldehyde and Formic Acid Levels in Blood and Urine in Man After Exposure to Formaldehyde. Zentralbl. Arbeitsmed. Arbeitsschultz Prophyl. 26:154-158 (Ger).

C-6. Exposure of humans to 0.78 mg HCHO/m^3 or avg. 1.28 mg HCHO/m^3 for 3 or 8 h, respectively. Levels of HCHO and HCOOH were measured in the blood and urine after exposure and after a recovery period. Weak experimental design due to lack of appropriate controls and smoking histories.

5-244 Elinek, R. 1974. Precancerous Laryngeal Diseases and Their Relation to Carcinoma. Acta Univ. Palacki. Olomuc. Fac. Med. 70:245-316 (Russ).

D-3. Exposure of 20 rats to formalin vapors (no HCHO concentrations given) for from 0.5 h to 32 d. Preparation of larynx histological sections from animals killed after 71 d from last exposure showed hypersecretory changes in 17 rats, significant chronic inflammatory infiltration in the membrane itself of 12 rats, dilation of the channels of the serous-mucous glands in 8 rats, and squamous cell metaplasia of the pseudostratified epithelia in 4.

5-134 Ettinger, L., and M. Jeremias. 1955. A Study of the Health Hazards Involved in Working with Flameproofed Fabrics. N. Y. State Dep. Labor Div. Ind. Hyg. Mon. Rev. 34(7):25-27.

C-4. Garment industry workers exposed to 1.25-13.75 mg HCHO/m^3 complained of eye, nose, and throat irritation. A brief, anecdotal account of the toxicity. A longer discussion of the treatment process, problems with it, and possible solutions.

5-174 Fassett, D. W. 1963. Aldehydes and Acetals. In: Industrial Hygiene and Toxicology, 2nd revised ed., F. A. Patty, D. W. Fassett, and D. D. Irish, Eds. Interscience Publishers, New York, New York. Vol. 2, pp. 1959-1989.

C--. Includes a specific review of the toxicity of HCHO: very mild eye and nose irritation at 2-3 ppm; increased irritation and lacrimation at 4-5 ppm, tolerated for 10-30 min; profuse lacrimation and barely tolerable irritation at 10 ppm; coughing, lacrimation, and difficulty breathing at 10-20 ppm, irritation lasting up to 1 h after exposure stops; and very serious injury following 5-10 min exposure to 50-100 ppm. The 30-min LC_{50} for acrolein in rats is 130 ppm.

5-236 Fel'dman, Yu. G. 1971. An Answer to K. K. Sidorov, Medical Science Candidate. Hyg. Sanit. 36(12):435-436.

D--. Reply to the criticisms of Sidorov (1971) [5-270]. Agrees that the workplace MPC for HCHO is 0.5 mg/m^3, but maintains that the one-time MPC for atmospheric air is 0.035 mg/m^3 and the mean diurnal MPC for atmospheric air is 0.012 mg/m^3. These figures are supported by U.S.S.R. (1972) [3-094].

5-007 Fel'dman, Yu. G. 1972. Biological Action of Certain Products from Atmospheric Photochemical Reactions. Gig. Sanit. 37(1):6-9 (Russ).

D-7 (animal). B-7 (human). For HCHO, the human odor threshold was 0.073 mg/m^3 and the threshold for effect on brain electrical activity was 0.053 mg/m^3. The bulk of the report considers the effect of mixtures of O_3, NO_2, and HCHO on humans and rats, the results indicating simple summation effects.

5-008 Fel'dman, Yu. G. 1974. Combined Action on the Human Organism of a Mixture of the Major Components of Automobile Exhaust Gases (Carbon Monoxide, Nitrogen Dioxide, Formaldehyde, and Hexane). Gig. Sanit. No. 10: 7-10 (Russ); English translation by Joint Publications Research Service, JPRS-65836, National Technical Information Service, U.S. Department of Commerce, Springfield, Va.

A-9. For HCHO, the subthreshold odor value was 0.054 mg/m^3 and the subthreshold EEG activity value was 0.04 mg/m^3. A good interaction study: a mixture of low concentrations of HCHO, NO_2, CO, and hexane was found to be simply additive in effect. The significance of the EEG effects is dubious.

5-048 Fel'dman, Yu. G., and T. I. Bonashevskaya. 1971. On the Effects of Low Concentrations of Formaldehyde. Hyg. Sanit. 36(5):174-80.

A-10. The human odor threshold was found to be 0.073 mg/m^3. EEG changes were induced by 0.053 mg/m^3. The recommended one-time maximum permissible concentration for atmospheric air was 0.04 mg/m^3. Chronic exposure of rats to 0.012-3 mg/m^3 caused mild functional and morphological changes at the higher levels, but no changes at 0.012 mg/m^3.

5-184 Fel'dman, Yu. G., and N. D. Eksler. 1975. Assessment of the Action of Atmospheric Pollution on the Electric Activity of the Brain. Gig. Sanit. No. 9:11-14 (Russ).

B-7. The EEG's of rabbits exposed to 0.65 mg HCHO/m^3 + flashing light for 20 min showed detrimental effects such as deterioration of the reactions of rearrangement of rhythm of all studied brain structures. In the same conditions, rabbits exposed to 0.035 mg HCHO/m^3 did not show any EEG changes. These tests are mentioned in Bokina and Eksler (1973) [5-003].

5-330 Fischer, M. H. 1905. The Toxic Effects of Formaldehyde and Formalin. J. Exp. Med. 6:487-518.

C-7. Inflammatory lung changes are described for animals (small numbers of various small and medium-size laboratory species) exposed to unquantitated HCHO levels (but apparently high; generated by common methods used for disinfection). These results contradict those of 9 earlier reports by workers who found no serious ill effects upon exposure of animals to disinfection levels of HCHO.

5-325 Freeman, H. G., and W. C. Grendon. 1971. Formaldehyde Detection and Control in the Wood Industry. For. Prod. J. 21(9):54-57.

D-3. A test for monitoring HCHO in the workplace and for checking the relative amounts of HCHO given off by different adhesives, was developed. Workers complained when levels were >1 ppm. HCHO was felt to be a contributor to increased accidents.

5-049 Frey, G., K.-H. Bock, H. Meister, H.-U. Haug, J. Kilian, and F. W. Ahnefeld. 1979. Effects of Ventilation with Defined Formaldehyde Concentrations on Lung Function and Lung Structures: Animal Experiments on the Noxiousness of Formaldehyde Residues after Disinfection in the Aseptor. Anesthesist 28(6):271-278.

B-12. Exposure of pigs to 0.03 to 2.5 mg HCHO/m^3 for 6 h. Similar respiratory effects at all three levels.

5-051 Gadzhiev, G. P., V. G. Deinega, V. V. Sukhanov, I. M. Levshina, N. T. Yarym-Agaeva, and G. A. Petrenko. 1977. Hygienic Evaluation of a New Technology of Methane and Dust Control in Coal Mines.

D-4. The physical conditions of miners in mines treated with urea-HCHO resin did not differ after several months from that of miners in untreated mines. In treated mines, the air contained 0.02-0.13 mg HCHO/m^3 and 0.14-0.8 mg MeOH/m^3 during cleaning operations. Rats given an intratracheal dose of treated or untreated dust showed more severe bronchial changes if the dust was followed by a 6-mo exposure to 0.5-0.6 mg HCHO/m^3 and 5.0-6.0 mg MeOH/m^3.

5-017 Galibin, G. P. 1963. Action of Hardened (meaning three-dimensional or cured) Synthetic Resins on Animal Systems. Toksikol. Nov. Prom. Khim. Veshchestv 5:45-50 (Russ).

D-7. Rats were exposed for 2 h/d for 12 d to decomposition products generated when various hardened synthetic resins were heated at 60°C; e.g., phenol-HCHO resin gave 0.5 mg phenol/m^3 and 0.2 mg HCHO/m^3. Behavior, threshold of excitability, and morphological composition of the blood showed no differences from those of the controls.

5-315 Gamble, J. F., A. J. McMichael, T. Williams, and M. Battigelli. 1976. Respiratory Function and Symptoms. An Environmental-Epidemiological Study of Rubber Workers Exposed to Phenol-Formaldehyde Type Resin. Am. Ind. Hyg. Assoc. J. 37:499-513.

C-9. The title workers were exposed to HCHO (mean 0.047 mg/m^3), NH_3 (mean 0.052 mg/m^3), resorcinol (mean 0.295 mg/m^3), and respirable particulates (<0.5 mg/m^3). There was an excess of self-reported symptoms of eye and respiratory tract irritation, but no difference in baseline lung function tests. Some acute, temporary "small airways" effects occurred after the workday.

5-284 Garry, V. F., L. Oatman, R. Pleus, and D. Gray. 1980. Formaldehyde in the Home. Some Environmental Disease Perspectives. Minn. Med. 63(2):107-111.

B-7. A study of 168 people exposed in their homes to 0.2-1.0 ppm HCHO, with no control or comparison group. Data are stratified by age of subject. Symptoms include respiratory problems, mucous membrane irritation, skin rash, and gastrointestinal complaints.

5-426 Geomet, Inc., and Technology and Economics, Inc. 1980. Mobile Home Evaluation of Formaldehyde Problems in Residential Mobile Home. Final Task 1 Report. PB81-175499, National Technical Information Service, U.S. Department of Commerce, Springfield, Virginia. 154 pp.

C--. Extensive review of HCHO properties, monitoring techniques, sources and emissions in mobile homes (0-4.2 ppm), human health effects, international standards, and abatement techniques.

5-295a Giulietti, M. A. 1980. Connecticut Department of Health Services, Preventable Diseases Division, Toxic Hazards Section, July 14, 1980 Summary Report [Urea Formaldehyde Insulation Investigations]; transmitted to MRI by M. A. Giulietti, Product Safety, Department of Consumer Protection, State of Connecticut. 5 pp.

B-6. The results of a study of 282 cases complaining of adverse health effects and living in buildings with urea-formaldehyde insulation (a total of 847 people questioned). Detectable HCHO levels ranged from 0.5 to 10 ppm. Symptoms included eye, nose, throat, and skin irritation, nausea, headache, and fatigue. Symptoms were reported (including odor perception) in buildings with nondetectable (<0.5 ppm) HCHO levels.

5-052 Gofmekler, V. A. 1968. Effect on Embryonic Development of Benzene and Formaldehyde in Inhalation Experiments. Hyg. Sanit 33(3):327-332.

D-5. Same study as Pushkina et al. (1968) [5-012] and Gofmekler et al. (1968) [5-238] on rats and progeny. Data on effect of exposure on fetal organ weights.

5-237 Gofmekler, V. A. 1974. Embryotropic Action of Chemical Atmospheric Pollution. Gig. Sanit. 39(9):7-10 (Russ); English translation available from John Crerar Library, Chicago, Illinois. Order No. 13535-06J.

D--. Review of teratology study of albino rats exposed continuously during pregnancy to 0.01 and 1.0 mg HCHO/m^3. Data tabulated from original article for this report.

5-185 Gofmekler, V. A., and T. I. Bonashevskaya. 1969. Experimental Studies of Teratogenic Properties of Formaldehyde, Based on Pathological Investigations. Gig. Sanit. 34(5):92-94 (Russ); Hyg. Sanit. 34(5):266-268.

D-5. Same study as Pushkina et al. (1968) [5-012], Gofmekler et al. (1968) [5-238], and Gofmekler (1968) [5-052] on rats and progeny. Data on histological and histochemical changes.

5-238 Gofmekler, V. A., N. N. Pushkina, and G. N. Klevtsova. 1968. Some Biochemical Aspects of the Embryotropic Effect of Benzene and Formaldehyde. Gig. Sanit. 33(7):96-98 (Russ); Hyg. Sanit. 33(7):112-116.

D-6. Same data on effect of HCHO exposure on ascorbic and nucleic acid levels in rats as Pushkina et al. (1968) [5-012].

5-054 Goloshchapov, O. D. 1979. Protein Metabolism in Experimental Formaldehyde Poisoning. Khim. Prom-st., Ser.: Toksikol. Sanit. Khim. Plastmass. No. 3:11 (Russ).

C-5. Rats exposed to 20 mg HCHO/m^3 for 6 wk were protected by a diet with 32% protein from the ensuing disturbances of protein metabolism seen in rats fed a normal ration with 18% protein. Compare Goloshchapov and Agranovskii (1976) [5-239].

5-239 Goloshchapov, O. D., and M. Z. Agranovskii. 1976. Lipoamide as a Component of a Prophylactic Diet in Exposure to Formaldehyde. Gig. Sanit. No. 3:25-28 (Russ).

C-11. Rats exposed to 20 mg HCHO/m^3 for 3 h/d for 6 wk were protected by a diet containing 5 mg lipoamide/kg from the disturbances seen in serum proteins and amino acids, ascorbic acid in the liver, behavior changes, depression in weight gain, dystrophic and necrotic changes in the liver, etc., in rats fed a diet with 18% protein without additional lipoamide.

5-403 Gosselin, R. E., H. C. Hodge, R. P. Smith, and M. N. Gleason. 1976. Formaldehyde. In: Clinical Toxicology of Commercial Products--Acute Poisoning. Fourth Edition. The Williams and Wilkins Co., Baltimore, Maryland. pp. 166-168.

D--. Brief review.

5-057 Granati, A., R. Lenzi, and E. Monaco. 1978. Environmental Health Problems in the Clothing Industry in Relation to Formaldehyde-Treated Fabrics. Riv. Med. Lav. Ig. Ind. 2(July-Sept.):221-232 (Ita).

B-9. Study of garment factory workers exposed to levels of HCHO up to ~ 0.5 mg/m^3. Of 3034 workers, 30.3% reported cutaneous and mucous membrane irritations. During the exposure period, there was an ~ 800% increase in symptoms and seriousness of irritation compared to previous period when different fabric (the source of the HCHO) was used.

5-240 Green, G. M., and D. Carolin. 1967. The Depressant Effect of Cigaret Smoke on the *in vitro* Antibacterial Activity of Alveolar Macrophages. N. Engl. J. Med. 276(8):421-427.

D--. HCHO at 1.6-163 µg/mL (levels above those found in cigarette smoke) did not inhibit the *in vitro* phagocytic ability of rabbit pulmonary alveolar macrophages. Whole cigarette smoke did.

5-361 Griesemer, R. A., A. G. Ulsamer, J. C. Arcos, J. R. Beall, et al.* 1980. Report of the Federal Panel on Formaldehyde. National Toxicology Program, Public Health Service, Department of Health and Human Services, Research Triangle Park, North Carolina. 64 pp.

A--. A very extensive and authoritative review and evaluation of animal and human exposure to try to determine the potential health risks to humans from chronic exposure to HCHO. The Panel concludes that ".....it is prudent to regard formaldehyde as posing a carcinogenic risk to humans." Conclusions on other topics such as teratogenicity/reproductive effects and animal-to-man data extrapolation are not made.

5-241 Guseva, V. A. 1972. Gonadotropic Effect of Formaldehyde on Male Rats During Its Simultaneous Introduction with Air and Water. Gig. Sanit. No. 10: 102-103 (Russ).

B-6. Male rats exposed for 6 mo to 0.5 mg HCHO/m^3 air and 0.1 mg HCHO/L orally for 4 h, 5x/wk produced normal nos. of normal offspring, but the content of nucleic acids in their testicles was significantly reduced.

5-186 Guseva, V. A. 1973. Effect of Formaldehyde During its Joint Respiratory and Oral Administration. Gig. Sanit. No. 5:7-11 (Russ).

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* See page A-4 for a complete listing of the panel members and their affiliations.

C-8. Exposure of rats simultaneously by inhalation (0.12, 0.25, or 0.5 mg/m^3) and ingestion (0.1, 0.01, or 0.005 mg/L) for 4 h/d, 5 d/wk, for 7 mo. Effects on CNS, conditioned reflex, biochemistry, pathomorphology, and neurohistology were studied. No effects seen at the combination of lowest doses.

5-394 Guzeev, Yu. M., and I. V. Bachinskii. 1980. Upper Airway Damage and Methods for Reducing the Worker Morbidity in the Woodworking Industry. Zh. Ushn., Nos. Gorl. Bolezn. No. 5:47-54 (Russ).

D--. Woodworking industry workers (512) were exposed to wood dusts, HCHO, toluene, xylene, abrasive dusts, and/or electrowelding dusts. Workers (185) exposed to the highest concentrations of HCHO (2.7 mg/m^3) but lower levels of wood dust (7.0 mg/m^3), abrasive dust (11.8 mg/m^3), and electrowelding aerosols (0.46 mg/m^3) had the lowest incidence of upper respiratory tract problems (7.0%). Of these patients, 30.7% showed hypertrophy of the mucous membranes, a higher incidence than in the other groups of workers exposed to less HCHO but more solvents and dusts.

5-363 Hanrahan, L. P., K. A. Dally, and H. A. Anderson. 1980. A Random Sample Survey of Wisconsin Mobile Homes: Formaldehyde Concentrations and Health Effects. Wisconsin Division of Health, Department of Health and Social Services, Madison, Wisconsin. 29 pp.

B-6. Two groups of mobile home residents (105 total) were studied. 23 different symptoms are reported, but only burning eyes was statistically associated with HCHO. Levels measured ranged from < 0.14 to 1.01 mg/m^3. An indoor HCHO standard of 0.2 ppm is recommended.

5-058 Harper, C., and J. M. Patel. 1978. Inactivation of Pulmonary Cytochrome P-450 by Aldehydes. Fed. Proc. 37(3):767.

D--. An abstract only, so no experimental details (levels and mode of exposure) are given. Formaldehyde caused destruction of liver microsomal P450 and pulmonary cytochrome P450 with no requirement for NADPH.

5-137 Harris, D. K. 1953. Health Problems in the Manufacture and Use of Plastics. Br. J. Ind. Med. 10:255-268.

D-7. Clinical examination of 25 men exposed to HCHO in a factory making urea-HCHO and phenol-HCHO resins and employed for > 5 y revealed abnormalities in blood counts in 13 and dyspnea in 4. Only 4 had been affected by dermatitis.

5-360 Harris, J. C., B. H. Rumack, and F. D. Aldrich. 1981. Toxicology of Urea Formaldehyde and Polyurethane Foam Insulation. J. Am. Med. Assoc. 245(3):243-246.

D-3. Review of the use and toxicity of urea-formaldehyde foam. Includes the results of questionnaires filled out by occupants of homes insulated with the foam, reporting dyspnea, headache, rhinitis, eye irritation, cough, and frequent colds. No HCHO levels given.

5-313 Helwig, N. 1977. How Safe Is Formaldehyde. Dtsch. Med. Woch. 102:1612-1613 (Ger); English translation available from John Crerar Library, Chicago, Illinois. Order No. 810412-06T.

C-4. Young school children exposed to ~ 5 ppm HCHO from HCHO-containing fiberboard for ~ 8 mo complained of irritation, nausea, and apathy. Habituation and individual variability in sensitivity were seen.

5-242 Hendrick, D. J., and D. J. Lane. 1975. Formalin Asthma in Hospital Staff. Br. Med. J. 1:607-608.

C-8. Inhalation provocation tests confirmed that exposure to formalin vapors was the cause of the delayed asthmatic symptoms in one hospital staff member but not the cause of change in ventilatory function of another member who had suffered from asthma as a child and hay fever since age 19.

5-060 Hendrick, D. J., and D. J. Lane 1977. Occupational Formalin Asthma. Br. J. Ind. Med. 34(1):11-18.

C-6. 8 cases of occupational asthma developed among 28 members of nursing staff at Hemodialysis Unit in which formalin was used to sterilize dialysis machine, over a 3-y period. 2 of 5 persons had positive responses to formalin provocation tests. No air sample measurements were requested, and no control or comparison group was studied.

5-061 Hollowell, C. D., J. V. Berk, C. Lin, W. W. Nazaroff, and G. W. Traynor. 1979a. Impact of Energy Conservation in Buildings on Health. LBL-9379, National Technical Information Service, Springfield, VA. 11 pp.

C--. At low ventilation rates, HCHO concentrations in indoor air are frequently > 0.1 mg/m^3 when outdoor concentrations are typically 0.02 mg/m^3. Indoor and outdoor HCHO concentrations and the health effects of HCHO are briefly reviewed.

5-062 Hollowell, C. G., J. V. Berk, C. I. Lin, and I. Turiel. 1979b. Indoor Air Quality in Energy-Efficient Buildings. Conf. 790523-2, National Technical Information Service, U.S. Dept. of Commerce, Springfield, VA. 12 pp.

C--. HCHO concentrations in an Energy Research House in Ames, Iowa, were 51-125 ppb indoors compared to < 5 ppb outdoors.

5-349 Hollowell, C. D., J. V. Berk, M. L. Boegel, R. R. Miksch, W. W. Nazaroff, and G. W. Traynor. 1980. Building Ventilation and Indoor Air Quality. Stud. Environ. Sci. 8(Atmos. Pollut.):387-396.

C--. Indoor air concentrations of HCHO reported from the U.S., Denmark, Sweden, and West Germany are frequently > 0.120 mg/m^3, which is the limit set for indoor air by the Netherlands in July 1978. HCHO concentrations in a test kitchen with a new gas stove ranged from 0.040 mg/m^3 when a hood vent with a fan was used at high speed to 0.460 mg/m^3 when no stove vent or hood was used. (The values reported for this study by Hollowell et al., 1979a [5-061] were 0.035 and 0.400 mg/m^3, respectively.) Typical outdoor HCHO concentration during the test was 0.005 mg/m^3.

5-009 Horton, A. W., R. Tye, and K. Stemmer. 1963. Experimental Carcinogenesis of the Lung. Inhalation of Gaseous Formaldehyde or an Aerosol of Coal Tar by C3H Mice. J. Natl. Cancer Inst. 30:31-43.

B-10. Acute and chronic exposure of mice to 50-900 mg HCHO/m^3 produced death and at lower levels tracheobronchial epithelium changes but no carcinomas. No mention of effects on nasal cavity.

5-140 Hovding, G. 1969. Occupational Dermatitis from Pyrolysis Products of Polythene. Acta Derm. Venereol. 49:147-149.

D-4. Case report of exposure to small amounts of smoke (presumably containing HCHO and acrolein) from cutting polyethylene bags. Symptoms of the skin and the mucous membranes of the eyes and upper respiratory tract were described. No measurements and no follow-up after changes in the ventilation system. All five workers gave a positive response to a patch test with a 4% aqueous HCHO solution.

-- Howlett, C. T., Jr. 1980. An Assessment of the Regulation of Indoor Air Quality. In: Proc. 14th Wash. State Univ. Int. Symp. Particleboard, Pullman, Washington, April 1980. pp. 145-158.

D--. General review. Includes some international regulations and recommendations for allowable HCHO levels.

5-065 Hsie, A. W., J. P. O'Neill, J. R. San Sebastian, D. B. Couch, J. C. Fusco, W. N. C. Sun, P. A. Brimer, R. Machanoff, J. C. Riddle, N. L. Forbes, and M. H. Hsie. 1978. Mutagenicity of Carcinogens: Study of 101 Agents in a Quantitative Mammalian Cell Mutation System, CHO/HGPRT. Fed. Proc. 37(6):1384.

B--. A standard Chinese hamser ovary bioassay for mutagenicity (CHO/HGPT) showed formaldehyde negative. The abstract called the result a "possible FALSE negative: with no data furnished.

5-366 Ikeda, A., Y. Horiguchi, and K. Koyoshi. 1980. Research on the Effect of Air Pollution. 2. Studies on Biological Effects of Carbohydrates. On Aldehydes. Kanagawa-ken Taiki Osen Chosa Kenkyu Hokoku 22:193-196 (Japan).

C-7. Exposure of rabbits to 6.3 mg/m^3 for 3-4 min caused decreased heart rate and respiratory HCHO movement and changes in blood pressure.

1-0172 ILO. 1970. Permissible Levels of Toxic Substances in the Working Environment. Occupational Safety and Health Series 20, International Labour Office, Geneva. pp. 194-198.

C--. Maximum acceptable concentrations in Czechoslovakia:

	Normal MAC (mg/m^3)	Short Single Exposure MAC (mg/m^3)
Acrolein	0.5	1.0
NH_3	40	80
HCHO	2	5
HCN	3	15
MeOH	100	500
H_2S	30	-

5-141 ILO/WHO Committee. 1970. Permissible Levels of Toxic Substances in the Working Environment--Sixth Session of the Joint ILO/WHO Committee, Occupational Health and Safety Series, Title 20. International Labor Office, Geneva. pp. 190, 201, 213, 242, 288, 290, 292, 295, 296, 306, 333, and 348.

C--. International values ranged from 0.5-20 ppm HCHO, with 5 ppm the most frequent standard for occupational exposure.

5-066 Ionescu, J., D. Marinescu, V. Tapu, and A. Eskenasy. 1978. Experimental Chronic Obstructive Lung Disease. I. Bronchopulmonary Changes Induced in Rabbits by Prolonged Exposure to Formaldehyde. Morphol. Embryol. (Bucur). 24(3):233-242.

C-5. Male rabbits exposed to aerosol of 3% of HCHO for 3 h/d for up to 50 d. No dose level given. In-depth discussion of changes induced in the respiratory system by the exposure.

5-067 Ishchenko, V. N., and I. K. Pushkina. 1978. Evaluation of the Working Conditions in the Manufacture and Processing of Phenol-Formaldehyde Resins. Gig. Sanit. No. 11:98-100 (Russ).

C-8. The workers were exposed to < 0.5 mg HCHO/m^3, phenol usually at > 5 mg/m^3 (its MAC), cresol (< MAC), high temperatures, and high humidity, and were involved in strenuous physical activities. Only the exposed women workers showed significant increases in morbidity, especially in respiratory diseases, musculoskeletal afflictions, and diseases of the urogenital system compared to the exposed men or the control men and women. Sleep disturbances were also more frequent in the exposed women. Domestic burdens were probably a contributing factor to the illnesses of the exposed women.

5-142 Iwanoff, N. 1911. On Some Aldehydes of Practical Importance. Arch. Hyg. 73:307-340 (Ger).

C-8. Acute exposure of cats to HCHO and acrolein. Study is of interest but of limited value because of high dose levels used ($\geqq$ 260 mg HCHO/m^3 and $\geqq$ 25 mg acrolein/m^3).

6-024 Jermini, C., and A. Weber. 1975. Air Pollution by Cigarette Smoke. Soz.-Praeventivmed. 20(5):213 (Ger).

C--. Smoking 10 tobacco cigarettes in a 30 m^3 room produced the following concentrations of irritating substances: acrolein, 0.120 ppm; HCHO, 0.450 ppm; CO, 24 ppm; and NO, 0.678 ppm. The corresponding MAC's are 0.1, 2, 50, and 25 ppm, respectively.

5-208 Jermini, C., A. Weber, and E. Grandjean. 1976. Quantitative Determination of Various Gas-Phase Components of the Side-Stream Smoke of Cigarettes in the Room Air as a Contribution to the Problem of Passive-Smoking. Int. Arch. Occup. Environ. Health 36(3):169-181 (Ger).

D--. An unventilated 30 m^3 room in which 30 cigarettes were smoked contained 0.37 ppm acrolein. The unpolluted air in the room contained 0.036 ppm HCHO, and 0.06 ppm HCHO after one cigarette was smoked. Other components were also measured.

5-246 Jordeczka, S., B. Basa, and S. Basa. 1973. The Incidence of Chronic Nonspecific Respiratory Disease Among the Workers of Furrier Industry. Abstr. Congr. Pol. Phthisjopneumonol. Soc. 18:100-101.

D--. Occupational study is confounded by exposures to NH_3, naphthalene, trichloroethylene, and acetic acid esters as well as HCHO and smoking. The respiratory disease was significantly correlated with duration of smoking habit but not with the number of cigarettes smoked daily.

5-209 Kabe, J. 1971. Bronchial Asthma and Asthma-Like Dyspnea Caused by Inhalation of Simple Chemicals. J. Allergol. 20(6):444-450 (Jap).

D--. Kabe defined four types of allergologic patterns caused by inhalation of low-molecular-weight compounds--immediate type, delayed type, non-allergic, and irritative type, as well as undetermined type reactions. When Kabe (1969) [Shonikagaku 10:513] administered dilute solutions of formalin to guinea pigs over long periods, a delayed increase in respiratory frequency was not induced as was observed when they inhaled other respiratory antigens.

5-247 Kalpazanov, Y., M. Stamenova, and G. Kurchatova. 1976. Air Pollution and the 1974-1975 Influenza Epidemic in Sofia: A Statistical Study. Environ. Res. 12(1):1-8.

D-5. Multiple regression analysis is used to study the influence of meteorological conditions and air pollutants on the number of influenza cases. Several pollutants were considered: dust, NO_x, oxidants, phenol, SO_2 and HCHO (0.0107-0.0145 mg/m^3). A statistically significant dependence was found between the number of ill during a given day and the concentration of HCHO 2 days earlier. Other relationships were seen for the other pollutants.

5-143 Kamchatnov, V. P., and S. S. Gayazova. 1971. Temperature Asymmetry in Workers Exposed to Formaldehyde Vapor. Hyg. Sanit. 86(1):286-287.

C-8. Exposure to 5-78 mg HCHO/m^3 for 5-20 y caused a pathological skin thermal asymmetry (0.6-2.2°C) which existed before a workday began in 48.4% of the workers and increased to 60% by the end of the workday. The authors consider this evidence of adverse CNS effects. Headache, vertigo, and irritability were also reported.

5-010 Kane, L., and Y. Alarie. 1977. Sensory Irritation to Formaldehyde and Acrolein During Single and Repeated Exposures in Mice. Am. Ind. Hyg. Assoc. J. 38:509-522.

B-12. Mice exposed to low levels of HCHO and acrolein in single and repeated acute exposures with decreases in respiration rate. Kane and Alarie recommend a TLV of 0.03 to 0.3 ppm HCHO.

6-069 Kane, L. E., and Y. Alarie. 1978. Evaluation of Sensory Irritation from Acrolein-Formaldehyde Mixtures. Am. Ind. Hyg. Assoc. J. 39(4):270-274.

B-10. A mathematical model applied to the data on the effects of acrolein and HCHO alone and in 11 combinations on the respiratory rate of mice indicates that competitive agonism exists between acrolein and HCHO when both are present.

3-134 Kane, L. E., C. S. Barrow, and Y. Alarie. 1979. A Short-Term Test to Predict Acceptable Levels of Exposure to Airborne Sensory Irritants. Am. Ind. Hyg. Assoc. J. 40(3):207-229.

D--. Review of short-term exposure studies with mice, involving HCHO, acrolein, and 9 other chemicals. Recommended highest concentration for an Air Quality Standard was 0.003 ppm HCHO.

5-071 Katz, G. V., and S. Laskin. 1977. Effect of Irritant Atmospheres on Macrophage Behavior. In: E.R.D.A. Symp. Ser. 43(Pulm. Macrophage Epithelial Cells):358-373. C. L. Sander, G. E. Dagle, and H. A. Ragan, Eds. Order No. Conf. 760927, Energy Research and Development Administration, National Technical Information Service, U.S. Department of Commerce, Springfield, VA.

C-7. Pulmonary alveolar macrophage activity of cells collected from rats pre-exposed to ~ 12.5 and ~ 25 mg HCHO/m^3. Higher level only decreased phagocytic activity.

5-190 Kensler, C., and S. P. Battista. 1963. Components of Cigarette Smoke with Ciliary-Depressant Activity. Their Selective Removal by Filters Containing Activated Charcoal. New Engl. J. Med. 296:1161-1166.

B-13. Technique described in minute detail - controls include points not addressed in other papers. Their 1966 article [5-248] that discussed recovery is important addition to this line of bioassay tests. Method of quantitating effect is hard to follow: what number of micrograms of gas per 1.2 liter "puff" of air (when 8 puffs are administered) is needed to produce 50% inhibition of tracer particles' movement of 5 mm on isolated rabbit trachea. For HCHO, this value was 6 μg, about three times the HCHO level in each puff of cigarette smoke.

5-248 Kensler, C. J., and S. P. Battista. 1966. Chemical and Physical Factors Affecting Mammalian Ciliary Activity. Amer. Rev. Resp. Dis. 93(3):93-102.

C-12. HCHO tested on isolated rabbit tracheal preparations produced reversible inhibition of ciliary activity, following 12-s exposures to unknown concentrations. The in vitro bioassay may have applicability to in vivo mammalian ciliary transport.

5-390 Kerfoot, E. J. 1972. Formaldehyde Vapor Emission Study in Embalming Rooms. The Director 42:6-7.

C-4. A summary of the information given in Kerfoot and Mooney (1975) [5-145].

5-145 Kerfoot, E. J., and T. F. Mooney, Jr. 1975. Formaldehyde and Paraformaldehyde Study in Funeral Homes. Am. Ind. Hyg. Assoc. J. 36:533-537.

B-4. Embalmers exposed to 0.11-6.58 mg HCHO/m^3 complained of eye and upper respiratory tract irritation. Some sinus problems and asthma reported. The necessity for adequate ventilation is demonstrated. No comparison group.

5-367 Kettner, H. 1978. Indoor Contamination by Chemical Substances and Their Hygienic Significance. In: Org. Verunreinig. Umwelt: Erkennen, Bewerten, Vermindern. K. Aurand, V. Haesselbarth, E. Lahmann, G. Muller, and W. Niemitz, Eds. Erich Schmidt Verlag, Berlin, Germany. pp. 448-453 (Ger).

C--. Maximum allowable indoor air concentrations in the USSR:

Acrolein	0.1 mg/m^3
NH_3	0.2
HCN	0.002
HCHO	0.01
MeOH	0.5

5-072 Kilburn, K. H., and W. N. McKenzie. 1978. Leukocyte Recruitment to Airways by Aldehyde-Carbon Combinations that Mimic Cigarette Smoke. Lab. Invest. 38(2):134-142.

B-11. Exposure of hamsters to HCHO and acrolein alone and with carbon particles. Effect only from combination of two and very high level HCHO. Significant in relation to exhaust mixture, especially diesel.

5-249 Kilburn, K. H., W. N. McKenzie, and R. J. Thurston. 1976. Effects of Formaldehyde, as Vapor and Absorbed [sic] on Carbon on Hamster Airways. Am. Rev. Respir. Dis. 113(4):238.

D--. Appears to be preliminary data on effect of HCHO alone and with carbon particle. Full study reported in Kilburn and McKenzie (1978) [5-072].

5-250 Kitchens, J. F., R. E. Casner, G. S. Edwards, W. E. Harward, II, and B. J. Macri. 1976. Investigation of Selected Potential Environmental Contaminants: Formaldehyde. PB-256839, National Technical Information Service, U.S. Dept. of Commerce, Springfield, VA. 217 pp.

C--. The authors review the potential environmental hazards of HCHO resulting from its manufacture, use, inadvertent production from combustion and other sources, and nascent sources such as paraformaldehyde, trioxane, and hexamethylenetetramine. Early literature on aldehyde (as HCHO) emissions from mobile sources reported values for automobiles of 3.3 to 18.7 lb/1,000 gal. (6,250 lb) gasoline. Diesel engines emit aldehydes at approx. the same rate and aircraft engines at about half their rate. This report pointed out that the automobile is the primary source of outdoor air pollution but that stationary combustion is also a main source of atmospheric HCHO. Irradiating the hydrocarbon-nitrogen oxide mixtures in auto exhaust leads to a threefold increase in the HCHO content.

5-433 Koivusalo, M. 1956. Studies on the Metabolism of Methanol and Formaldehyde in the Animal Organism. Acta. Physiol. Scand. Suppl. 131.39:1-103.

D--. A review of early literature plus several *in vivo* and *in vitro* experiments on the metabolism of MeOH and HCHO. So much work has been done in the past 25 years on the topic, it was not used as a reference.

5-074 Kok, G. L. 1979. Analytical Instrumentation for the Determination of Formaldehyde in the Ambient Atmosphere. Abstract No. 9.0672. Toxicology Research Projects Directory 4(9):1-75.

C--. Since current methods for determining HCHO in ambient air at its usual concentrations (~ 10 ppb, which is ~ 0.015 mg/m^3) are not sensitive enough, this research project is developing a new method based on the chemiluminescent reaction of gallic acid with HCHO.

5-075 Kopylova, L. S., S. E. Gle'iberman, T. V. Likhtman, T. F. Semenova, and M. I. Alekseeva. 1980. Safety Study of a Method for Disinfecting Artificial Pulmonary Ventilation Apparatus with Aerosols Containing Formaldehyde. Anesteziol. Reanimatol. No. 2:33-37 (Russ).

D--. Aerosols of a sterilizing mixture containing 20% HCHO, 30% ethanol, and 50% chaladone-12 (CCl_2F_2) at concentrations 2-74 g/m^3 irritated the mucosae of the upper respiratory tract of albino rats exposed for 45-90 min. Guinea pigs exposed to the mixture at 2 mg/m^3 for 2 mo were sensitized to HCHO. Rats were exposed to the residual gases (+ NH_3) [$\leqq$ 0.2 mg/m^3] in the artificial ventilation apparatus for up to 30 d, but no hematological or morphological changes were observed compared to the controls.

5-147 Krans, E. W. 1935. Effects of Fumes during the Moulding of Certain Types of Plastics. Ind. Med. Surg. 4:10-11.

D-6. A 29-y-old workman exposed to fumes in the unmolding of articles produced from a formaldehyde-based resin developed a typical bronchial cough after a few mo. Three years later, he developed pneumonia, from which he recovered within ~ 3 mo. Krans suggested that lung infections are likely when the membranes have been hardened due to continual HCHO inhalation exposure.

5-343 Krasevac, J. 1972. Influence of Anatomical and Occupational Factors on Respiratory Allergy of the Upper Respiratory Organs. Med. Glas. 26(6):138-141 (Serbo-Croat).

D--. Workers in the wood-forming industry were exposed to wood dust, lye, and nitro dyes as well as HCHO. No exposure levels given.

5-148 Kratochvil, I. 1971. The Effect of Formaldehyde on the Health of Workers Employed in the Production of Crease Resistant Ready Made Dresses. Pr. Lek. 23:374-375. (Cze).

D-5. A description of symptoms following suspected exposure to HCHO (no measurements were made) for up to 7 y: light conjunctivitis in 72%, rhinopharyngitis in 28%, and chronic bronchitis in 22%. The small number of workers (18) further limits the usefulness of this study.

5-252 Kulle, T. J., and G. P. Copper. 1975. Effects of Formaldehyde and Ozone on the Trigeminal Nasal Sensory System. Arch. Environ. Health 30(5):237-243.

C-11. Study of nasal sensory response in guinea pigs exposed to ~ 0.6 to 3.2 mg/m^3 HCHO. Sensory response decreased with HCHO exposure and only partially recovered after exposure.

5-321 Kuz'menko, N. M., A. I. Buslenko, S. E. Kataeva, T. I. Kravchenko, and R. S. Asatryan. 1975. Sensitizing Effect of Formaldehyde During Production of Plastics. Vrach. Delo No. 6:131-134 (Russ).

C-4. Workers were exposed to 0.025-0.22 mg HCHO/m^3 and dust and had direct contact with phenol-HCHO powders. Half had 4-5 y and half > 5 y of service. 8% had clinical changes in the skin. 22% were sensitized by skin applications of aqueous HCHO. Some cases had a general reaction of headaches, weakness, and poor health 2-3 d following HCHO application to the skin. Lack of controls greatly reduces the usefulness of this study.

5-353 LaBelle, C. W., J. E. Long, and E. E. Christofano. 1955. Synergistic Effects of Aerosols. Particulates as Carriers of Toxic Vapors. A.M.A. Arch. Ind. Health 11:297-304.

C-6. Acute exposure of mice to HCHO and acrolein in combination with various aerosols. In general, aerosols increased the toxicity of HCHO and had no effect on acrolein.

5-149 Leonardos, G., D. Kendall, and N. Barnard. 1969. Odor Threshold Determinations of 53 Odorant Chemicals. J. Air Pollut. Control Assoc. 19(2): 91-95. Data also appear in A.D. Little, Inc., Research on Chemical Odors, Manufacturing Chemists Association, Washington, D.C. 1968.

A-11. Definitive paper. The odor recognition thresholds for various compounds were:

NH_3	46.8 ppm
H_2S	0.00047 ppm
H_2S (from Na_2S)	0.0047 ppm
HCHO	1.0 ppm
Acrolein	0.21 ppm
Methanol	100 ppm

5-400 Lin, C., R. N. Anaclerio, D. W. Anthon, L. Z. Fanning, and C. D. Hollowell. 1979. Indoor/Outdoor Measuremtns of Formaldehyde and Total Aldehydes. LBL-9397, Conf-790917-10, or EEB-Vent-79-7, National Technical Information Service, U.S. Department of Commerce, Springfield, VA. 14 pp.

C--. Analytical methods are described, and information given in earlier report of this series is repeated.

5-382 Long, K. 1979. Problems Associated with the Use of Urea-Formaldehyde Foam for Residential Use. Department of Energy Publication No. ORNL/SUB-7559/1, U.S. Department of Energy Information Center Complex, U.S. Department of Energy, Oak Ridge, Tennessee. 86 pp.

D--. Foams samples were tested in chambers for HCHO emissions. Increases were found for higher temperatures (7°C vs. 33°C) and higher humidities (> 80% vs. < 75%). Emission decreased with time (1-43 d). The entire range of values detected was 0.15-13.69 ppm.

5-078 Loomis, T. A. 1979. Formaldehyde Toxicity. Arch. Pathol. Lab. Med. 103(7):321-324.

C--. Good basic review of acute actions (primary irritant effect and the immunogenic-mediated response). The authors suggest that, based on the insufficient data available, exposure to $\leqq 0.5$ ppm for several hours is a dose without detectable toxic effects.

5-316 Ludwig, H. 1935. Acute Formaldehyde Bronchiolitis in Workman Handling Artificial Resin. Samml. Vergiftungsfallen. 6:227-230 (Ger).

C-4. This paper describes the onset and course of the acute bronchiolitis (asthma, slimy sputum, etc.) with eczema and fever observed in a 38-y-old chemically sensitive workman who had been exposed to urea-HCHO resin powder while unloading drums containing the resin. The inhaled resin particles may have released HCHO in the lungs and probably exacerbated the response due to HCHO by producing mechanical irritation of the bronchi.

5-079 Lyne, A. R. 1979. Inhalation of Formaldehyde Vapor (letter). Br. Med. J. 2(6204):1589.

C--. The TLV (ceiling) for HCHO in workplace air in Great Britain is 2 ppm (same as that of the ACGIH in the U.S.A.).

7-071 Makar, A. B., and T. R. Tephly. 1977. Methanol Poisoning VI: Role of Folic Acid in the Production of Methanol Poisoning in the Rat. J. Toxicol. Environ. Health. 2(5):1201-1209.

D--. Rats placed on a folate-deficient diet for 10-12 wk showed a marked sensitivity to methanol poisoning. Formate oxidation was inhibited so that high blood formate and acidosis occurred. HCHO did not accumulate appreciably, however, in the acidotic rats.

5-080 Makeicheva, N. A. 1978. Data for the Hygienic Standardization of a Mixture of Furfural, Formaldehyde, Phenol and Acteone, in the Atmosphere. Gig. Sanit. No. 9:3-7 (Russ).

B-9. Human odor threshold (0.077 mg/m^3) and electrocortical conditioned reflex threshold (0.034 mg/m^3) for HCHO were determined. Recommended a one-time MAC of 0.035 mg $HCHO/m^3$ in the atmospheric air.

5-253 Markova, Z. S., and A. I. Sautin. 1975. Hygienic Evaluation of Textile Products According to Questionnaire Data. Gig. Sanit. 7:118-119 (Russ).

A-7. The numbers of complaints decreased and their character changed in 627 of 1,000 salespersons exposed to fabrics finished with HCHO resins with increasing length of service. The aging factor may have influenced the results. Complaints independent of length of service were pains in the heart, mucus discharge, sleep disturbance, dyspnea, angina, and nausea. Sales persons contacting unfinished linen fabrics registered far fewer complaints.

5-327 Marshall, F. J. 1980. New Jersey State Department of Health. Special Epidemiology Project. Health Investigations of Urea-Formaldehyde Foam December 1977 to January 1980. New Jersey State Health Department, Trenton, New Jersey. 11 pp.

B-6. Residents of homes with urea-formaldehyde foam installed 1-40 mo earlier complained of odor, mucous membrane and skin irritation, and problems sleeping. Ambient air levels ranged from 0 to 0.98 mg $HCHO/m^3$.

5-290 Matanoski, G. M. 1980. Epidemiologic Study of Mortality in Pathologists. From an annotated list of epidemiologic and formaldehyde monitoring studies prepared by the Epidemiology Branch, Health Review Division, Environmental Protection Agency.

D--. Very brief description of a current research project. Data to date show increased mortality due to kidney and liver cancer, and decreased oral pharyngeal carcinomas. No HCHO levels.

5-082 Matsumura, T., and E. Higuchi. 1979. Concentration of Formaldehyde in Urban Air. Kogai To Taisaku. 15(12):1547-1550 (Japan).

C-9. Levels of HCHO in air over Tokyo were measured continuously for 9 y. Reports incident on June 28, 1971, in which HCHO levels ranged from ~ 10 to ~ 40 ppb with ~ 12 h above 20 ppb. (Mean value of 9-y period was 7.1 ppb). Thousands reported eye irritation that day. The hourly values over the 9 y ranged from 1 to 73 ppb, with 45.8% of the total hourly measurements ≤ 5 ppb. Fluctuations during the day, wk, mo, and year are discussed.

5-083 Matsushima, T., D. Mizoguchi, and R. Soejima. 1978. Experimental Mouse Pneumonia Following Lung Injury with One Percent Formaldehyde. Kawasaki Med. J. 4(1):35-46.

C-11. Study of bacterial pneumonia, caused by *Serratia marcescens*, in albino mice. HCHO was used to injure the respiratory tract to make the mice susceptible to infection. All mice exposed to 1% (10,000 ppm) HCHO developed pneumonia when exposed to bacteria whereas few mice unexposed to HCHO did.

7-074 McMartin, K. E., G. Martin-Amat, P. E. Noker, and T. R. Tephly. 1979. Lack of a Role for Formaldehyde in Methanol Poisoning in the Monkey. Biochem. Pharmacol. 28(5):645-650.

D--. Formic acid appears to be the major metabolic agent responsible for methanol toxicity in the monkey since formic acid accounts for the acidosis and the ocular symptoms.

5-085 Mecler, F. J. 1978. Biochemical Changes Seen in Guinea Pigs after Inhalation of Formaldehyde and Nitrogen Dioxide. Toxicol. Appl. Pharmacol. 45(1):298-299.

D-4. Repeated dose study of effect of $\sim$ 12.5 mg HCHO/m^3 exposure on lung, liver, and kidney glutathione and glutathione reductase levels.

5-192 Melekhina, V. P. 1960. Maximum Permissible Concentration of Formaldehyde in Atmospheric Air. USSR Literature on Air Pollution and Related Occupational Diseases 3:135-140.

A-9. Same data as Melekhina (1964) [5-193] in a more condensed form, with some of the experimental details not given, but also containing some not in the other article.

5-193 Melekhina, V. P. 1964. Hygienic Evaluation of Formaldehyde as an Atmospheric Air Pollutant. In: USSR Literature on Air Pollution and Related Occupational Diseases-A Survey. NTIS TT64-11574, National Technical Information Service, U.S. Department of Commerce, Springfield, VA. 9 pp.

A-9. Human odor threshold (0.07 mg/m^3), light sensitivity threshold (0.098 mg/m^3), and respiratory frequency threshold ($<$ 2.5 mg/m^3) were determined. Atmospheric levels near a formalin production plant were 0.0055-1.5 mg HCHO/m^3 and caused some irritation. The exhaust gases of gasoline engines contained 6-9 mg HCHO/m^3. Air samples collected 1-2 m from street during max. evening traffic contained 2-10 mg HCHO/m,^{3} avg. 2.6 mg/m^3. 24-h samples collected 7-8 m from heavily travelled streets generally contained 0.001-0.0068 mg HCHO/m^3, with a max. of 0.017 mg/m^3.

5-155 Miller, B. H., and H. P. Blejer. 1966. Report of an Occupational Health Study of Formaldehyde Concentrations at Maximes, 400 E. Colorado Street, Pasadena, California. Report No. S-1838, State of California Health and Welfare Agency, Dept. of Public Health, Bureau of Occupational Health, Los Angeles, California. 5 pp.

C-3. HCHO levels in a dress store, due to treated fabrics, ranged from 1.1 to 4.1 mg/m^3. Odor and mild eye irritation reported. Possible additive effect with smog.

5-086 Misiakiewicz, Z., G. Szulinska, A. Chyba, and E. Czyz. 1977. Effect of Formaldehyde on the Development of Rats During Long-Term Continuous Exposure. Rocz. Panstw. Zakl. Hig. 28(1):99-106 (Pol).

C-7. Two-generation study on effects of 1.0 mg HCHO/m^3 on rats exposed continuously for 8 mo (including during pregnancy) and on offspring also exposed continuously for 8 mo. No changes in blood parameters, smaller increase in body wt. increase in second generation and of relative liver wt. Upper respiratory tract morphological changes in exposed rats.

5-156 Morrill, E. E. 1961. Formaldehyde Exposure from Paper Process Solved by Air Sampling and Current Studies. Air Cond. Heat Vent. 58(7):94-95.

C-4. Workers exposed to 0.9-1.6 ppm HCHO and a trace of NH_3 complained of itching eyes, dry and sore throats, disturbed sleep, and unusual thirst upon first awakening.

5-388 Most, R. S., G. R. Curry, A. V. Sardinas, and J. S. Marks. 1981. Persistence of Symptoms Associated with Urea-Formaldehyde Foam Insulation. J. Environ. Health 43(5):251-253.

B-5. A follow-up to the study by Giuletti (1980). Of the households originally complaining of adverse health effects, 72 still had symptoms at least as severe as ~ 2 y earlier. The avg. foam-age in these homes was 2.3 y. No new HCHO measurements were made. 38 no longer had any symptoms, for a variety of reasons. No control group.

5-158 Murphy, S.D., and C. E. Ulrich. 1964. Multi-Animal Test System for Measuring Effects of Irritant Gases and Vapors on Respiratory Function of Guinea Pigs. Am. Ind. Hyg. Assoc. J. 25:28-36.

D-5. Methods development study reporting limited data on effect of 5.9 and 18.8 mg HCHO/m^3 on guinea pig respiration.

5-157 Murphy, S. D., H. V. Davis, and V. L. Zaratzian. 1964. Biochemical Effects in Rats from Irritating Air Contaminants. Toxicol. Appl. Pharmacol. 6:520-528.

C-8. Study of effect of acrolein (1-4 ppm, 20-81 h) and 18-h, 35 ppm HCHO exposure on rat organ weights and alkaline phosphatase activity. The same values for concentration x time for acrolein had different effects, the continuous exposures to the higher concentrations causing increased liver wt. and enzyme activity.

5-213 Nagornyi, P. A. 1971. Evaluation of a Combined Effect Exerted by Several Factors by the Method of Multiple Regression. Farmakol. Toksikol. 34(3):366-369 (Russ).

D-8. Nagornyi used multiple regression to process the results of 2-h lethality studies in mice with 13 different mixtures of phenol, toluene, anthracene, and HCHO (resulting from thermo-oxidative decomposition of a resin based on the constituents). The results indicated that the mixture was synergistic, the mixture being many times more toxic than the separate components. By eliminating HCHO from the mixture, N. calculated that its LC_{50} in mice would be 91 mg/m^3.

5-254 Nagornyi, P. A. 1973. Combined Action of Several Factors Studied by Regression Analysis. Gig. Sanit. No. 7:76-82 (Russ).

D-8. Nagornyi (1973) continues the work of Nagornyi (1971) with tests of 20 new mixtures with and without HCHO. The results here from its elimination from mixtures indicate that the LC_{50} of HCHO is 155 mg/m^3.

5-091 Nagornyi, P. A. 1977. Hygienic Evaluation of Working Conditions and Health Status of Workers in the Production of Phenol-Formaldehyde Polymers. Gig. Tr. Resp. Mezhved. Sb. No. 13:48-52 (Russ).

C-5. Workers were exposed to phenol and HCHO in concentrations of 0.9-43 mg/m^3 and 0.9-11.5 mg/m^3 respectively, as well as to aerosols of lead (0.006-0.06 mg/m^3) and resin dust (2.1-9.0; MAC = 6 mg/m^3) Morbidity among the plant workers, studied for 12 y, was mostly due to respiratory illnesses, which was significantly more elevated in years of grippe epidemics and was higher than the sick rate seen in mine and metal workers. The incidences of women showing complications of pregnancy, labor, and the post-natal period were not reported although incidences were reported for practically every other sickness or symptom.

5-090 Nagornyi, P. A. 1978. Harmful Action of Formaldehyde in Low Concentrations (a Review of the Literature). Gig. Tr. Prof. Zabol. No. 6:42-44 (Russ).

C--. Review of Russian human and animal studies.

5-089 Nagornyi, P. A. 1979. Comparative Evaluation of Some Methods for Studying the Characteristics of the Combined Effect of Mixtures of Chemical Substances in Critical Tests. Deposited Doc. VINITI 836-79. 15 pp (Russ).

C-8. Two mathematical treatments were used to process data obtained from acute exposures of mice to 53 mixtures of phenol plus HCHO. Pure HCHO at ≦ 120 mg/m^3 and pure phenol at ≦ 75 mg/m^3 did not kill any mice during a 2-h dynamic poisoning test. Calculated LC$_{50}$'s and LC$_{100}$'s were 505 ± 64 and 1,030 mg/m^3 for HCHO and 177 ± 11 and 278 mg/m^3 for phenol. The mixtures had a synergistic action being 1.03-2.2x more toxic than equal concentrations of phenol or HCHO alone.

-- Nagornyi, P. A., R. K. Mel'nichenko, Zh. A. Sudakova, and L. L. Filipchenko. 1975. Toxicity and Maximum Permissible Concentration of a Complex Set of the Neoleucorite (Phenol-Formaldehyde) Resin Volatile Products. Gig. Tr. Prof. Zabol: No. *:from TOXLINE abstract.

D--. Animals exposed to 0.75 mg HCH/m^3 plus 0.26 mg phenol/m^3 and to 0.13 mg HCHO/m^3 plus 0.11 mg phenol/m^3 showed functional and morphological changes in the internal organs and systems, some of which had not been reversed after a 1-mo recovery period. A mixture of 0.05 mg HCHO/m^3 plus 0.06 mg phenol/m^3 produced insignificant, fully reversible changes in the test animals. N. recommends 0.01 mg/m^3 each HCHO and phenol as the MACs when present together in the workplace.

5-092 Nagornyi, P. A., Z. A. Sudakova, and S. M. Shchablenko. 1979. General Toxic and Allergenic Action of Formaldehyde. Gig. Tr. Prof. Zabol. No. 1:27-30 (Russ); English translation available from John Crerar Library, Chicago, Illinois. Order No. 79-127-93-06J.

B-9. Chronic exposure of albino rats and guinea pigs to 0.5 mg/m^3 of HCHO. General health unaffected, some blood and urine parameters affected.

5-323 Nefedov, Yu. G., V. P. Savina, N. L. Sokolov, and V. E. Ryzhkova. 1969. Contaminants in the Air Exhaled by Man. Kosm. Biol. Med. 3(5):71-77 (Russ).

D--. Total aldehyde concentrations in exhaled breath of 10 smokers ranged from not detected to 0.09 mg/m^3 and in the breath of 11 nonsmokers, from not detected to 0.12 mg/m^3. The people were healthy and were aged 25 to 35 years.

5-376 Nelson, N. 1979. Written Communication from New York University Medical Center, Institute of Environmental Medicine to NIOSH, Rockville, Maryland; cited in NIOSH/OSHA (1980). p. 5.

B-7. Of 100 rats exposed for 6 h/d for 544 d to ~ 12.5 mg HCHO/m^3 along with 10.6 ppm HCl, 25% developed squamous cell carcinomas of the nasal cavity within 814 d of the 1st exposure. These cancers are not typically produced by bis(chloromethyl) ether, the reaction product of HCHO and HCl.

5-255 Neshkov, N. S., and A. M. Nosko. 1976. Effect of Toxic Components of Fiber Glass-Reinforced Plastics on the Higher Nervous Activity and Sexual Function of Males. Gig. Tr. 12:92-94 (Russ).

D--. Fifty-eight of 143 workers exposed to phenol, HCHO, aniline, styrene, and other contaminants at 1.5x the MAC complained of sexual and pyschoneurological disorders. See the discussion of this paper by Griesemer et al. (1980), p. 44. They concluded, "It is impossible to determine how much of the sexual dysfunction might be attributable to formaldehyde since appropriate control groups were not included and these workers were exposed to a variety of toxic chemicals in addition to formaldehyde."

6-124 Newsome, J. R., V. Norman, and V. L. Zaratzian. 1965. Vapor Phase Analysis of Cigarette Smoke. Tob. Sci. 9:102-110; or Tobacco 161(4): 24-32.

D--. Levels in tobacco smoke (μg/40 ml puff):

	Unfiltered	Filtered
methanol	13	10
HCHO	4.1	3.6
acrolein	8.2	7.9
HCN	32	29
H_2S	3.4	3.1
NH_3	12	13

5-375 NIOSH/OSHA, National Institute for Occupational Safety and Health/ Occupational Safety and Health Administration. 1980. Current Intelligence Bulletin 34. Formaldehyde: Evidence of Carcinogenicity. National Institute for Occupational Safety and Health, U.S. Department of Health and Human Services, and Occupational Safety and Health Administration, U.S. Department of Labor.

C--. Recent animal work on the carcinogenicity of HCHO is reviewed with 27 references, some of them unpublished. NIOSH and OSHA recommend that HCHO be handled as a potential occupational carcinogen.

5-318 Nova, M. M., and R. G. Touraine. 1957. Asthma from Formaldehyde. Arch. Mal. Prof. 18:293-294 (Fre).

D-7. Case history of a North African man working for 2 y in a factory handling fatty acids, HCHO, and various other aldehydes. After 1 y, he had skin eruptions attributed to the acids. After 1-2 mo working in a room with HCHO vapors, he suffered from vomiting, headache, and respiratory difficulty typical of pulmonary edema lasting ~ 1 wk. In the following days, he developed dyspnea, and then the characteristics of chronic, recurrent asthma. No HCHO levels given. Includes a brief review of other occupational exposures, distinguishing between those causing irritation and edema, isolated asthma crises after each exposure, and chronic asthma even after all exposure stops.

5-352 NRC, National Research Council Panel on Vapor-Phase Organic Pollutants. 1976. Vapor-Phase Organic Pollutants. Volatile Hydrocarbons and Oxidation Products. Printing and Publishing Office, National Academy of Sciences, Washington, D.C. 417 pp

C--. An authoritative, but brief, review of various aspects of acrolein and HCHO health effects literature is included in appropriate chapters of this book, which was used as a source of additional pertinent original papers.

5-331 NRC, National Research Council; Committee on Toxicology. 1980. Formaldehyde - An Assessment of Its Health Effects. AD-A087854, National Technical Information Service, U.S. Department of Commerce, Springfield, VA. 45 pp.

A--. Extensive review of animal and human exposure to HCHO, through all routes. From the results of 2 controlled human experimental studies, the Committee predicts that at < 0.25 ppm HCHO, $< 20\%$ of the population will experience minimal to slight eye, nose, and throat irritation, and recommends "...maintaining formaldehyde at the lowest practical concentration to minimize adverse effects on public health." Includes a list of world-wide recommended and promulgated HCHO exposure limits for outdoor ambient air (0.008-0.1 ppm), indoor air (0.1-0.4 ppm), and occupational air (0.4-10 ppm).

5-093 Okawada, N., I. Mizoguchi, and T. Ishiguro. 1979. Effects of Photochemical Air Pollution on the Human Eye - Concerning Eye Irritation, Tear Lysozyme and Tear pH. Nagoya J. Med. Sci. 41(1-4):9-20.

A-11. 0.2 ppm HCHO was the threshold for eye irritation during 300 s exposures. Moderate to severe irritation was caused by 0.5-1.0 ppm.

5-194 Ostapovich, I. K. 1975. Characteristics of the Sensitizing Action of Sulfur Dioxide and Formaldehyde in Various Regimes of Their Inhalation. Gig. Sanit. No. 2:9-13 (Russ).

B-6. Rats and guinea pigs were continuously exposed to HCHO at 2, 7, and 15 mg/m^3. Guinea pigs were also exposed intermittently to 7 mg/m^3. The time to toxic effects and to allergic effects, if any, increased with decreasing concentration. At higher levels, the toxic effects superceded the allergic effects, but allergic effects appeared sooner at a continuous level of 2 mg $HCHO/m^3$ or when the avg. concn. was 2.3 mg/m^3 due to the intermittency of the 7 mg/m^3 exposures.

5-391 Ostapovich, I. K. 1978. Some Methodical Approaches to Regulating the Content of Chemical Allergens in the Air. Gig. Aspekty Okhrany Okruzh. Sredy, (Moskva) No. 6:84-85 (Russ).

B-6. The experimental results presumably of Ostapovich (1975) [5-199] (although another, lower concentration--0.5 mg HCHO/m^3--is mentioned here) with respect to the allergic effects on rats and guinea pigs gave a straight line on a log scale grid. By extrapolation and the use of a nomogram (no figures given), Ostapovich calculated an inactive concentration for HCHO of 0.003 mg/m^3.

5-256 Otte, W., and K. Kroepelin. 1973. Histological Changes in Guinea Pig Lungs after Formaldehyde Inhalation and x-Radiation and the Effect of Dexamethasone 21-isonicotinate Thereon. Arzneim.-Forsch. 23(3):420-424 (Ger).

D-6. Study of guinea pigs exposed to HCHO and x-radiation to irritate the lungs. Dexamethasone 21-isonicotinate reduced inflammation of lungs

5-257 Ozhiganova, V. N., L. A. Dueva, and N. G. Popova. 1976. Clinical Picture and Diagnosis of Occupational Bronchial Asthma Caused by Formaldehyde-Containing Polymers. Gig. Tr. Prof. Zabol. No. 11:17-20 (Russ).

C-10. The incidence of bronchial asthma, 34 of 972, in workers engaged in the production and processing of HCHO-containing polymers, was no higher than that in the general population. Various diagnostic methods differentiated those whose bronchial asthma was and was not due to HCHO. Most appeared to be sensitized in varying degrees to HCHO as were those showing disorders of bronchial potency (9). All should be removed from HCHO contact.

5-377 Ozhiganova, V. N., I. S. Ivanova, and L. A. Deuva. 1977. Bronchial Asthma in Radio Equipment Assemblers. Sov. Med. (Moscow) No. 4: 139-141 (Russ).

C-8. Bronchial asthma in radio equipment assemblers was usually due to the occupational exposure to HCHO (no concentration determined), a thermal destruction product of the rosin used in the lead soldering process. Methods are described to distinguish occupational from nonoccupational bronchial asthma.

7-076 Palese, M., and T. R. Tephly. 1975. Metabolism of Formate in the Rat. J. Toxicol. Environ. Health 1(1):13-24.

D--. The folate-dependent one-carbon pool plays a major role in the metabolism of formate to CO_2. Folate-deficient rats rely on the catalase-peroxidative system.

5-314 Paliard, F., L. Roche, C. Exbrayat, and E. Sprunck. 1949. Chronic Asthma Due to Formaldehyde. Arch. Mal. Prof. 10:528-530 (Fre).

D--. Case history of a man developing severe asthma-like symptoms after working 25 y in a tannery, which included continuous exposure to formaldehyde vapors. Irritation of the upper airways and conjunctiva, coughing, tramitis, loss of sense of smell, and dyspnea and cyanosis even at rest were observed. Some symptoms were not characteristic of asthma, and the authors attribute the problems to formaldehyde. Other facts, such as an apparent lack of sensitivity to HCHO, argue against this. No levels were given.

5-258 Pankova, V. B. 1976. Cytological Profile of the Lower Nasal Cavity Mucosa Under the Effect of Different Chemical Allergens. Deposited Doc. No. VINITI 2969-76:20-22 (Russ).

D--. Formalin was directly applied to the mucosa of the lower nasal cavity.

5-259 Patterson, R. M., M. I. Bornstein, and E. Garshick. 1976. Assessment of Formaldehyde as a Potential Air Pollution Problem. PB-258360, National Technical Information Service, Springfield, VA. 29 pp.

D--. The document contains a 5-page uncritical review of health effects literature on HCHO.

5-260 Pavlenko, S. M., and V. A. Guseva. 1973a. Dynamics of the Development of Adaptive Reactions Under the Long-Term Effect of Industrial Poisons Entering an Organism by Different Means. Itogi Nauki Tekh. Farmakol., Khimioter. Sredstva, Toksikol., Probl. Toksikol. 5:110-119 (Russ).

D--. The elaborate set of tests performed on rats exposed to low levels of HCHO, C_2H_5OH, CH_3OH, CCl_4, or cyclohexanone given by inhalation and/or by mouth does not distinguish the effects caused by each poison, i.e., they each elicit the same responses at nearly the same times.

7-042 Pavlenko, S. M., and V. A. Guseva. 1973b. Development of Adaptive Shifts after Complex Administrations of Nonelectrolyte Poisons. Gig. Sanit. No. 1:15-20 (Russ).

D--. This is a slightly different version of Pavlenko and Guseva (1973a) [5-260].

5-261 Pavlenko, S. M., T. V. Yudina, and V. A. Guseva. 1975. Methodological Approaches to an Evaluation of Latent Reactions of Certain Regulatory Systems of the Body in the Case of Different Ways of Intake of Toxic Substances. Gig. Sanit. No. 10:55-60 (Russ).

D--. Another abstruse study much like Pavlenko and Guseva (1973a) [5-260], wherein the effects of oral or inhaled HCHO are not especially different from those seen from low levels of C_2H_5OH, CH_3OH, CCl_4, or cyclohexanone.

5-399 Pendergast, H. 1979. Formaldehyde. A Basic Building Block of Industry. Formaldehyde Institute, Scarsdale, New York. 13 pp.

C--. This brief report summarizes work on HCHO recently done or begun by OSHA, NIOSH, EPA, the Dept. of Housing and Development, CPSC, and DOE and summarizes that "no valid scientific evidence was found to suggest that HCHO poses significant risk to human health or the environment." The report also describes the committees of the Formaldehyde Institute (Medical, Technical, Regulatory Action, and Information Resources and Communications) as well as the initiation of the HCHO inhalation carcinogenicity testing with rats and mice by the Chemical Industry Institute of Toxicology (CIIT).

5-095 Plunkett, E. R., and T. Barbela. 1977. Are Embalmer's at Risk? Am. J. Hyg. 38(1):61-62.

C-4. Embalmers exposed to unknown levels of HCHO reported eye, skin, and upper respiratory tract irritation. Some had acute bronchitis and others chronic bronchitis. Those without bronchitis had longer work histories. No control group.

5-096 Pod"yacheva, N. A. 1977. Generally Toxic Effect of Low Concentrations of Phenol and Formaldehyde During their Separate and Combined Effect on Experimental Animals. Gig. Aspekty Okhr. Zdorov'ya Naseleniya. p. 131 (Russ).

C-9. Exposing female rats to either HCHO or phenol at 0.5 mg/m^3 for 4 h/d for 4 mo increased the activities of cholinesterase, oxidase, and glutaminoaspartic aminotransferase and lowered the nucleic acid and total protein content of the serum while increasing SGOT and lowering the activities of cholinesterase and aspartic transferase in liver homogenates. These changes apparent within 2-3.4 mo, but when a mixture of 0.25 mg/m^3 of each compound was used, the changes appeared within 15-30 d.

5-159 Porter, J. A. H. 1975. Acute Respiratory Distress Following Formalin Inhalation. Lancet 2(7935):603-604.

C-8. A 27-y-old neurology resident during his second stint of preparing brain specimens using formalin noted irritation of the conjunctiva and nasal mucosa and became progressively dyspneic even at rest within 15 h after the exposure to a "high concentration of formaldehyde vapor." Chest x-ray showed increased interstitial markings with early edema. The clinical picture was that of acute pneumonitis that required treatment by aminophylline and steroids before recovery by 5 wk after the onset. The reaction may have been due to hypersensitivity, since the man experienced allergic rhinitis on exposure to common inhalation allergens.

5-262 Prave, V. E., M. M. Prupis, L. G. Cherniakova, B. L. Litvak, and A. P. Beliaeva. 1972. Health Evaluation of the Atmosphere in Working Premises of Disinfection Chambers. Gig. Sanit. 37(1):96-98 (Russ).

C-7. The subjects were exposed only to HCHO at concentrations of 0.33-42.0 mg/m^3. The incidences of various diseases of the respiratory system, skin, nervous system, liver, etc., as well as of cholinesterase inhibition are given but not compared to exposure levels or to the corresponding incidences among a control group.

5-404 Prigoda, Yu. G. 1973. Hygienic Characteristics of Air Conditions on Some Types of Automobile Highways. Aktual. Vopr. Gig. Naselennykh Mest, Mater. Vses. Konf. Molodykh Uchenykh. pp. 108-110 (Russ); Chem. Abstr. 1975. 82:076650a.

C--. HCHO concentrations along two USSR highways were 0.1-1.2 mg/m^3, whereas at a distance of 10-15 m from the highways the values were 0.005-0.15 mg/m^3.

6-115 Protsenko, G. A., V. I. Danilov, A. N. Timchenko, A. V. Nenartovich, V. I. Trubilko, and V. A. Sauchenkov. 1973. Working Conditions When Metals to which Primer has been Applied are Welded Evaluated from the Health and Hygiene Aspect. Avt. Svarka 26(2):65-68.

D--. Levels of many gases were determined under several different welding conditions: acrolein, 0.11-1.04 mg/m^3; and HCHO, 0.31-0.83 mg/m^3.

5-098 Pruett, J. J., H. Scheuenstuhl, D. Michaeli, and Z. Nevo. 1980. The Incorporation and Localization of Aldehydes (Highly Reactive Cigarette Smoke Components) into Cellular Fractions of Cultured Human Lung Cells. Arch. Environ. Health 35(1):15-20.

C--. Human fetal lung fibroblasts were incubated with trace amounts of ^{14}C-labeled HCHO for 10 min. The HCHO migrated into the nucleus, where the RNA fraction had the highest amount of HCHO.

5-012 Pushkina, N. N., V. A. Gofmekler, and G. N. Klevtsova. 1968. Changes in Content of Ascorbic Acid and Nucleic Acids Produced by Benzene and Formaldehyde. Bull. Exp. Biol. Med. 66:868-870.

D-6. Study of exposure of 0.012 and 1.0 mg/m^3 of HCHO on female rats and their fetuses caused decreased ascorbic acid levels.

5-195 Renzetti, N., and R. Bryan. 1961. Atmospheric Sampling for Aldehydes and Eye Irritation in Los Angeles Smog. J. Air Pollut. Control Assoc. 11(9):421-424 and 427.

D-10. An attempt at correlating eye irritation and aldehyde levels in smog. Total aldehydes ranged from 0.02 to 0.40 ppm; formaldehyde from 0 to 0.13 ppm. Good correlation was found for a log-probit relationship with total aldehydes, but the fit for HCHO wasn't as good.

5-196 Renzetti, N., and E. A. Schuck. 1961. Preliminary Observations on the Relationship Between Eye Irritation in Synthetic Systems and in the Atmosphere. J. Air Pollut. Control Assoc. 11(3):121-124.

C-8. Moderate to very severe (lacrimation in > 50% of the subjects) eye irritation was caused by 5-min exposure to 3 ppm HCHO. Comparisons are made to irritation caused by irradiated hydrocarbon/NO_2 mixtures and to outdoor smog conditions, in an attempt to show that HCHO and acrolein are the primary irritants in smog.

5-099 Rosenkranz, H. S. 1972. Formaldehyde as a Possible Carcinogen. Bull. Environ. Contam. Toxicol. 8(4):242-244.

C-2. In addition to the fact that formaldehyde has been known, from literature citations, to be a mutagen, the author now believes it to be a potential carcinogen. He used a microbial assay method with an E. coli strain that lacks DNA polymerase (involved in DNA repair). After the addition of an unknown amount of HCHO, to cultures grown in petri dishes, the zone of growth inhibition was 62 mm vs. 59 mm for the normal strain. Article lacks details, numbers of tests, ranges of results, and control information.

5-335 Rumack, B. H. 1978. Position Paper: Urea-Formaldehyde Foam. Rocky Mountain Poison Center, Denver, Colorado. 30 pp.

C--. This paper reviews toxicity problems, and consumer complaints related to urea-HCHO foam insulation as well as current standards and criteria for HCHO in workplace and ambient air. Other domestic sources of HCHO are enumerated: particle board, chipboard, wood panels, curtain and rug backings, auto exhaust, wood preservatives, smoking, fireplaces, possibly gas furnaces and appliances, glues, and permanent press fabrics. The Netherlands has promulgated a standard for homes insulated with urea-HCHO foam products -- $\leqq$ 0.5 ppm at 2 wk after foaming and 0.02 ppm after 2 mo.

5-344 Ryzhik, L. A. 1970. Hygienic Characterization of Foliated Hetinax Production. Gig. Tr. Prof. Zabol. 14(5):12-15 (Russ).

D--. Workers were exposed to cresol and HCHO in concentrations less than the maximum allowable concentration (MAC) as well as acetone ($\leqq$ 20 x > MAC), NH_3 ($\leqq$ 3 mg/m^3; MAC = 20 mg/m^3), and phenol ($\leqq$ 3 x > MAC). The health of the workers was not discussed.

5-160 Sachs, O. 1921. On Acute Dermatitis Caused by Vapors of Carbolic Acid, Formaldehyde and Ammonia in the Production of Synthetic Resins. Wien. Klin. Wochenschr. No. 29:356 (Ger).

D-3. Case reports of 8 workers with acute dermatitis of the face, forearms, and hands. Some conjunctivitis, bronchitis, and irritation of the nose. Problems are attributed to carbolic acid, NH_3, and HCHO, 3 of several compounds used in production. No air sampling done, or concentrations reported.

5-264 Saindelle, A., F. Ruff, N. Flavian, and J. L. Parrot. 1968. Histamine Release by Short-Chain Aldehydes. C. R. Hebd. Seances Acad. Sci., Ser. D. 266(2):139-140 (Fre).

D-3. Guinea pig lung fragments were incubated for 15 min in a solution containing 0.1 mg HCHO/mL, and 0-2.3 μg histamine/g was released. Other short-chain aldehydes were studied, with acetaldehyde being the most active in causing the release of histamine.

5-265 Sakula, A. 1975. Formalin Asthma in Hospital Laboratory Staff. Lancet 2:816.

D-6. Formalin vapor caused bronchial asthma in a 57-y-old hospital laboratory technician who prepared pathological specimens and histological sections.

5-161 Salem, H., and H. Cullumbine. 1960. Inhalation Toxicities of Some Aldehydes. Toxicol. Appl. Pharmacol. 2:183-187.

C-6. Exposure of mice, guinea pigs and rabbits to HCHO and acrolein in both vapor and aerosol form for up to 10 h HCHO concentrations of 19-20 mg/m^3 caused few deaths during exposure but a number of the animals died later. Acrolein at mean concentration of 4,624 to 5,225 mg/m^3 was lethal to all the animals in < 1 h. Mice were more susceptible to both HCHO and acrolein than other animals.

5-389 Samitova, R. Sh., Yu. P. Gracheva, and F. M. Gaynutdinov. 1973. Physiological-Hygienic Evaluation of Work Conditions and Gynecological Morbidity of Polishers of Formalin Departments of Fur Production. Nauchn. Trudy Kazansk. Med. In-ta. 42:37-42 (Russ).

C-10. By the end of the shifts, workers exposed to 2.0-7.5 mg HCHO/m^3, dust, methanol, ethanol, and formic acid (the last 3 at < MAC's) had complaints of vertigo, stimulation, noise in the ears, and decreased endurance. Small increases in some gynecological complaints were reported.

5-266 Sanotskii, I. V., V. N. Fomenko, G. A. Sheveleva, L. S. Sal'nikova, M. V. Nakoryakova, and T. E. Pavlova. 1976. A Study on the Effects of Pregnancy on the Sensitivity of Animals to Chemical Agents. Gig. Tr. Prof. Zabol No. 1:25-28 (Russ); English translation available from John Crerar Library, Chicago, Illinois. Order No. 80-11975-06J.

B-8. Study of the effect of pregnancy on the sensitivity of rats to HCHO. Levels of 0.4 to 6 mg/m^3 effected blood hemoglobin and liver and kidney functioning.

5-100 Sanotskii, I. V., V. N. Fomenko, L. S. Sal'nikova, and G. A. Sheveleva. 1977. Some Problems Related to Experimental Research of the Embryotropic Action of Industrial Chemical Compounds. Gig. Tr. Prof. Zabol. No. 2:27-30 (Russ).

C--. A review without full citations of work done at the Institute of Industrial Hygiene and Occupational Diseases of the Academy of Medical Science of the USSR. It is reported here without attribution that HCHO at levels up to and at the MAC were without effect on human embryogenesis of pregnancy whether exposure was at the 1st or 2nd month or the entire course.

5-312 Sardinas, A. V., R. S. Most, M. A. Giulietti, and P. Honchar. 1979. Health Effects Associated with Urea-Formaldehyde Foam Insulation in Connecticut. J. Environ. Health 41:270-272.

C-6. A preliminary report (of 69 complaints) of the full study discussed in Giulietti (1980) [5-295a]. Attempted to show differences in symptoms between those exposed to < 0.5 ppm and those exposed to 0.5-10 ppm: skin and miscellaneous symptoms were higher in the less exposed group, eye irritation and headache were higher in the high exposure group, and nose, throat, lung, and gastrointestinal tract irritation were about equal. These ratios changed in the full report, with the high exposure group reporting slightly higher symptoms in all categories.

5-162 Saury, A., M. P. Ravault, and V. Vincent. 1965. Optic Atrophy Due to Exposure to Formol Vapors. Bull. Med. Tox. Med. Leg. 8: 466-469 (Fre).

D--. Case history of a man suffering from optical neuritis, including blurriness and loss of vision. Because of the lack of any other findings, the authors attribute it to the man's exposure on the job while handling fabrics treated with a formaldehyde-containing mixture to prevent wrinkling. No levels are given and the cause-effect relationship is not definitely established.

7-501 Schneck, S. A. 1979. Methyl Aclohol. In: Handbook of Clinical Neurology, Vol. 36, Intoxications of the Nervous System, Part I. P. J. Vinken, and C. W. Bruyn, Eds. Elsevier/North-Holland, Inc. New York, New York. pp. 351-360.

D--. A good review of methanol poisoning and the presumed role of HCHO.

5-013 Schoenberg, J. B., and C. A. Mitchell. 1975. Airway Disease Caused by Phenolic (Phenol-Formaldehyde) Resin Exposure. Arch. Environ. Health 30:574-577.

C-9. Employees were exposed to phenol (7-10 mg/m^3) and HCHO (0.5-16.3 mg/m^3). A high proportion reported acute respiratory symptoms, but only small decreases in pulmonary functions during the work week were found. Employment for > 5 y caused lower pulmonary functions than shorter employment but those employees also had greater cigarette consumption (in pack-years).

5-101 Schreiber, H., M. Bibbo, G. L. Wied, G. Saccomanno, and P. Nettesheim. 1979. Bronchial Metaplasia as a Benign or Premalignant Lesion. I. Cytologic and Ultrastructural Discrimination Between Acute Carcinogen Effects and Toxin-Induced Changes. Acta Cytol. (Baltimore) 23(6):496-503.

C-8. Study of cytologic and histologic changes in tracheobronchial epithelium of hamster exposure to 312.5 mg/m^3. HCHO effects compared to changes in hamsters exposed to known carcinogens. Results indicated that HCHO is non-carcinogenic.

5-328 Schuck, E. A., and G. J. Doyle. 1959. Photooxidation of Hydrocarbons in Mixtures Containing Oxides of Nitrogen and Sulfur Dioxide. Report No. 29. Air Pollution Foundation. San Marino, California. pp. 41-46.

C-8. Same data as Schuck and Renzetti (1960) [5-307].

5-307 Schuck, E., and N. Renzetti. 1960. Eye Irritants Formed During Photooxidation of Hydrocarbons in the Presence of Oxides of Nitrogen. Air Pollut. Control Assoc. J. 10:389-392.

C-8. Moderate to severe eye irritation was caused by 5-min exposure to 1.5 ppm acrolein or 4 ppm HCHO. These 2 irritants accounted for most of the observed eye irritation caused by the products of the photooxidation of hydrocarbons with oxides of nitrogen. 3 ppm propionaldehyde and 10 ppm acetaldehyde caused no eye irritation.

5-163 Schuck, E. A., E. R. Stephens, and J. T. Middleton. 1966. Eye Irritation Response at Low Concentrations of Irritants. Arch. Environ. Health 13:570-575.

D-10. Exposure to the products of the irradiation of hydrocarbons/NO_2 mixtures caused eye irritation. Good correlation was seen with HCHO when it was present at $\geqq 0.3$ ppm, but not when it was < 0.3 ppm.

5-418 Selikoff, I. J., and E. C. Hammond. 1981. Carcinogenicity of Formaldehyde. Final Report. Report to the American Cancer Society by the Environmental Cancer Information Unit, Environmental Sciences Laboratory, Mt. Sinai School of Medicine, City University of New York, New York, New York.

C--. This 9-page report is bound with full copies of Griesemer et al. (1980) [Report of the Federal Panel on Formaldehyde] and NIOSH/OSHA (1980) [Formaldehyde: Evidence of Carcinogenicity]. In an earlier report the authors had raised the question of whether the nasal cancers seen in the CIIT study (Swenberg et al., 1980) were due to the combined effects of a viral infection and HCHO. In this report, they decide on the basis of the 24-mo results that

"HCHO exposure and not the viral infection appears to be the crucial factor in development of nasal carcinomas in the CIIT study." They recommend that since "cancer occurred in animals at levels not unlike those which can be found in some human exposures that "effective controls should be initiated to reduce or eliminate human exposures to HCHO."

5-198 Sgibnev, A. K. 1968. Influence of Small Concentrations of Formaldehyde Vapors on the Human Organism. Gig. Tr. Prof. Zabol. 12(7): 20-25 (Russ); English translation available from John Crerar Library, Chicago, Illinois. Order No. 74-13624-06J.

A-7. Exposure of humans to 0.3-0.4 or 1.0 mg/m^3 for 10 min caused slight respiratory and skin changes at the lower level and more extensive changes at the upper level. 1 mg/m^3 is recommended as the maximum permissible concentration.

5-014 Shafaiziev, U., and G. Shipovskikh. 1972. Working Conditions and Health of Workers Employed in Processing of Plastic Resins in Uzbekistan. Vop. Sanit. Gig. Usloviyakh Zharkaogo Klimata Usb. 1972:136-138 (Russ).

C-6. Workers were exposed to $\leqq$ 2-15.6 mg phenol/m^3 and 0.6-3.1 mg HCHO/m^3 as well as phenol-HCHO resin dust. Disturbances were seen more often in the pressmen, who were exposed to the higher resin dust concentrations, than in the polishers. Disturbances observed included chronic rhinopharyngitis (5 pressmen), skin irritations, stabbing-constricting pain in the heart region, muffling of heart tones at the tip, a tendency toward hypotonia (50%), gastritis and colitis, liver function disturbances, and nervous system disturbances in 24 of the 30 pressmen.

5-337 Sheveleva, G. A. 1971. Specific Action of Formaldehyde on the Embryogeny and Progeny of White Rats. Toksikol. Nov. Prom. Khim. Veschestv. 12:78-86; English translation available from John Crerar Library, Chicago, Illinois. Order No. 73-13539-06P.

B-11. Study of the effect of 0.5 to 5 mg HCHO/m^3 on pregnant rats and development and health of progeny.

5-164 Shipkovitz, H. D., 1968. Formaldehyde Vapor Emissions in the Permanent-Press Fabrics Industry. Report No. TR-52, Environmental Control Administration, Consumer Protection and Environmental Health Service, Public Health Service, U.S. Department of Health, Education and Welfare, Cincinnati, Ohio. 20 pp.

C-5. Formaldehyde concentrations during cutting, sewing, pressing, and storing of permanent press fabrics ranged in eight plants from not detected to 2.7 ppm. In two plants with good ventilation and two with fair ventilation, 5-15% of the employees showed respiratory and other complaints. In the four other plants with fair ventilation, such complaints came from > 15% of the employees.

5-018 Shumilina, A. V. 1975. Menstrual and Reproductive Functions in Workers with Occupational Exposure to Formaldehyde. Gig. Tr. Prof. Zabol. 75(12):18-21 (Russ); English translation available from John Crerar Library, Chicago, Illinois. Order No. 78-12467-06J.

B-8. Chronic exposure to 1.5-4.5 mg HCHO/m^3 or to 0.05-0.70 mg HCHO/ m^3 caused increased numbers of menstrual problems, genital diseases, problems during pregnancy and birth, and lower neonatal weights.

5-345 Sidorenko, G. I., F. F. Lampert, I. A. Pinigina, V. A. Klebanova, V. P. Osintseva, and A. F. Nazarenko. 1972. Experimental Substantiation of Air Sanitation Measures in Gas Supplied Apartments. Gig. Sanit. 37(7):24-28 (Russ).

D-8. Male rats exposed for 3 or 6 h/d for 125 d to 0.043 mg HCHO/ m^3, 0.07 mg C_6H_6/m^3, 0.44 mg NO_2/m^3, and 0.60 mg NO/m^3 (products of incomplete combustion of gas from a cooking stove) showed absence of weight gain, leukocytosis, increase in carboxyhemoglobin, CNS disturbance, and changes in the parenchymatous organs that were probably due to chronic CO poisoning. The emphysematous changes with atelectasis in the lungs were probably due to poisoning by the N oxides.

5-270 Sidorov, K. K. 1971. Letter to the Editor: Effect of Low Concentrations of Formaldehyde on the Organism. Hyg. Sanit. 36(12): 435.

D--. Corrections of the official standards given in the text of Fel'dman and Bonashevskaya (1971) [5-048]. The maximum permissible concentration of HCHO in a work zone was 0.5 mg/m^3.

5-178 Sim, V. M., and R. E. Pattle. 1957. Effect of Possible Smog Irritants on Human Subjects. J. Am. Med. Assoc. 165:1908-1913.

B-9. A study of acute ($\leqq$ 30 min) human exposure to several compounds of interest: HCHO at 17.3 mg/m^3 was slightly irritating; acrolein at 1.88 or 2.80 mg/m^3 was extremely irritating; acetaldehyde at 240 mg/m^3 was mildly irritating; and propionaldehyde at 324 mg/m^3 was mildly irritating. A more complex study of H_2SO_4 exposure was done.

5-165 Skog, E. 1950. A Toxicological Investigation of Lower Aliphatic Aldehydes--I. Toxicity of Formaldehyde, Acetaldehyde, Propionaldehyde, and Butyraldehyde, as well as of Acrolein and Crotonaldehyde. Acta Pharmacol. Toxicol. 6:299-318.

B-10. Acute exposure of rats to 600-1,700 mg HCHO/m^3 led to an LD_{50} of 1,000 mg/m^3. Rats exposed to 100 to 700 mg acrolein/m^3 showed an LD_{50} of 300 mg/m^3. This is a solid acute, lethal dose study.

5-392 Skvortsova, R. I., V. M. Puznyakovskii, and S. A. Rudakov. 1980. State of Some Metabolic Functions in Workers Manufacturing Phenol-Formaldehyde Resins. Gig. Sanit. No. 8:69-71 (Russ).

C--. This appears to be a fairly good occupational study, but because the end point studied (lowering of the acetylation of sulfanilamide by CoA) is not clearly a toxic effect, it was not rated by a pharmacologist or epidemiologist or tabulated. The authors ascribe the effect to phenol's blocking of the SH group of CoA (the site where the Ac group is attached), but the blocking action could arguably be attributed more to HCHO on the basis of their ordinary chemistry. Interestingly, the lowering of acetylation activity was most marked in 25-30-y-old female instrument workers (female "apparatchiks" were the most sensitive of phenol-HCHO resin workers in the study by Ishchenko and Pushkina, 1978 [5-067]) and press foremen.

5-272 Smirnova, N. A., and N. P. Granik. 1971. Remote After-Effects of Acute Occupational Lesions of the Respiratory Tract Caused by Irritating Gases. Gig. Tr. Prof. Zabol. 15(11):16-19 (Russ).

D--. Nothing specific is related about the four workers who were acutely poisoned by HCHO. Pneumosclerosis, bronchitis, and emphysema were seen as late effects in 35 of the 88 chemical plant workers, who were variously exposed to Cl_2 (46), HCl (2), $COCl_2$ (9), NO_x (11), $Ni(CO)_4$ (14), HCHO (4), and NH_3 (2).

5-104 Sprince, H., C. M. Parker, and G. G. Smith. 1979. Comparison of Protection by L-Ascorbic Acid, L-Cysteine, and Adrenergic-Blocking Agents against Acetaldehyde, Acrolein, and Formaldehyde Toxicity: Implications in Smoking. Agents Actions 9(4):407-414.

D-12. Rats were orally intubated with ~ 90% of the 24-h LD_{50} of HCHO or acrolein. Both groups gradually showed lethargy, tremors, respiratory distress, and death, which suggested that the primary toxic effect even through oral dosing was on the respiratory system. Lung congestion and pulmonary edema at death, are mentioned but there is no description of histopathology or even gross necropsy.

5-306 Stephens, E., E. Darley, O. Taylor, and C. Scott. 1961. Photochemical Reaction Products in Air Pollution. Int. J. Air Water Pollut. 4:79-100.

A-9. Eye exposure only to 1-5 ppm HCHO for 5 or 12 min caused moderate to severe irritation, the percentage of people affected varying with concentration, exposure time, and exposure conditions.

5-286 Stofft, E., I. Nitsche, and A. Mayet. 1971. Formaldehyde Content of the Air in Dissecting Rooms. Zentralbl. Bakteriol. Parasitenkd. Infektionskr. Hyg. Erste. Abt. Orig. Reihe. B. Hyg. Praev. Med. 155(2):131-141 (Ger).

D--. In dissection rooms, concentrations of HCHO over the fixed dead bodies were as high as 20 mg/m^3. Concentrations of $\leqq$ 10-100 mg/m^3 were typical in the area where the dead bodies were stored in conserving tubs.

5-338 Stupfel, M. 1976. Recent Advances in Investigations of Toxicity of Automotive Exhaust. Environ. Health Perspect. 17:253-285.

D--. Summary of levels of various components of exhaust: HCHO in gasoline exhaust (10-300 ppm), HCHO in diesel exhaust (5-30 ppm), HCHO in urban polluted air (0.05-0.12 ppm), HCHO in tobacco smoke (120 ppm), acrolein in urban polluted air (0.01 ppm), acrolein in tobacco smoke (60 ppm), and HCN in tobacco smoke (300-1,500 ppm). Extensive review of epidemiology and human and animal experimental results of exposure to exhaust.

5-405 Styazhkin, V. M., G. M. Kuznetsova, and T. P. Soldatchenkova. 1976. Hygienic-Chemical Study of an Experimental Mobile Home Made with the Extensive Use of Plastics. Gig. Aspekty Okhr. Okruzhayushchei Sredy. pp. 62-64 (Russ); Chem. Abstr. 1978. 89:203319w.

C--. The interior air concentrations of HCHO, NH_3, phthalate esters, and phenol (0.3, 1.1, 3.8, and 0.03 mg/m^3, respectively) in this mobile home made it unsuitable for human habitation.

5-106 Suga, K., S. Aoki, Y. Yasufuku, J. Nishikawa, and K. Yoshikawa. 1978. Survey of Ambient Air in Ohtsu Area in 1976. Shigakenritsu Eisei Kenkyusho Ho 12:162-173 (Japan).

C--. Ambient air samples in October 1976 from the Ohtsu area of Japan contained 0.009-0.018 mg HCHO/m^3, 0.0085 mg NH_3/m^3, and 0.0007-0.0015 mg H_2S/m^3.

5-362 Swenberg, J. A., W. D. Kerns, R. I. Mitchell, E. J. Gralla, and K. L. Pavkov. 1980. Induction of Squamous Cell Carcinoma of the Rat Nasal Cavity by Inhalation Exposure to Formaldehyde Vapor. Cancer Res. 40:3398-3402.

B-15. Rats were exposed to 2.1, 5.6, and 14.1 ppm HCHO for 6 h/d, 5 d/wk for 18 mo of a 24-mo study. Exposure to 14.1 ppm for up to 18 mo resulted in nasal cavity carcinomas. No tumors at lower levels. This is the experiment sponsored by the Chemical Industry Institute of Toxicology.

5-351 Taft, R. M. 1980. Hazard Evaluation and Technical Assistance Report No. TA 78-46, Potomac Village Shopping Center, Potomac, Maryland. PB80-150717, National Technical Information Service, U. S. Department of Commerce, Springfield, VA. 17 pp.

C-2. The tenants, employees, and customers of the shopping center complained of eye, nose, and throat irritation (no skin irritation) during 7 mo. Formaldehyde levels averaged ~ 1.4 mg/m^3, and probably emanated from urea-formaldehyde foam insulation, which had been removed 2 wk before.

5-215 Takhirov, M. T. 1974. Combined Action of Six Air Pollutants on the Human Body. Gig. Sanit. No. 5:100-102 (Russ); Chem. Abstr. 1974. 81:110854.

B-8. The odor threshold of HCHO was 0.065 mg/m^3. In studies of mixtures of HCHO, AcOH, Ac_2O, HCl, acetone, and phenol, simple summation effect was observed at low concentration, suggesting that during their simultaneous presence their total concentrations expressed in fractions of existing standards of each isolated substance should not exceed 1.

7-058 Teplyakov, S. D., V. A. Sokolova, G. G. Antipova, L. N. Zimont and R. A. Druz. 1980. Complex Assessment of Working Conditions in the Use of Cold-Setting Mixes with Urea-Furan Binder BS-40. Liteinoe Proizvod. No. 6:27-28 (Russ).

D-9. Workers were exposed to 0.1-1.2 mg HCHO/m^3, dust, and benzopyrene. Clinical examination in 1976 did not reveal any expressed pathological changes. A study published earlier of presumably the same workers by Chernomorskii et al. (1978) found respiratory pathology and functional changes. That study found slightly higher HCHO levels (2 mg/m^3), dust (10x the MAC), phenol, methanol, aldehydes, cyanides, and CO.

5-326 Thun, M. J., M. F. Lakat, and R. Altman. 1980. New Jersey Urea Formaldehyde Foam Insulation Study. New Jersey State Health Department, Trenton, New Jersey (currently undergoing revisions for publication).

C-13. A study of 395 households with recently installed urea-formaldehyde foam insulation. There was no excess of increased overall morbidity, although there was for 2 specific symptoms (skin burning and wheezing or breathing difficulty). Those households reporting persistent odor problems also reported the most health problems. Evidence of acute health effects is suggestive rather than conclusive. No HCHO levels given.

5-285 Timm, W., and P. M. Smith. 1979. Formaldehyde Odor and Health Problems Within Residences. Proc. Int. Conf. Therm. Insul. 1:223-248.

D--. A review attempting to refute the evidence that formaldehyde from foam insulation and particle board causes adverse health effects. It considers: lack of methods given for HCHO testing, the low incidence of complaints compared to the no. of homes insulated, over-reaction by the media and the public, other sources of HCHO exposure, and studies showing no evidence of toxicity at low HCHO levels. A threshold level for HCHO in residences of 0.5 ppm is recommended as being well below the safe toxic limit.

5-274 Tiunov, L. A., and V. A. Ivanova. 1976. The Effect of Some Industrial Poisons on DNAse Activity. Gig. Tr. Prof. Zabol. No. 1:29-34 (Russ).

B-8. DNA-ase levels in the liver were significantly increased when rats were exposed to 0.1, 0.7, or 3.9 mg HCHO/m^3 for 60 d. Levels in the spleen, however, were increased only for the highest HCHO concentration and decreased at 0.1 or 0.7 mg/m^3.

5-402 Tremer, H. M., H. L. Falk, and P. Kotin. 1959. Effect of Air Pollutants on Ciliated Mucous-Secreting Epithelium. J. Nat. Cancer Inst. 23(5):979-997.

D-8. Methods developments for measuring effect of various atmospheric contaminants on respiratory epithelium *in vitro*. Sections of the ciliated epithelium of the esophageal tract of the leopard frog were exposed to 1.1-3.3 mg HCHO or 0.4-1.4 mg MeOH in aerosols. Mucus flow was inhibited by HCHO and accelerated by MeOH.

5-324 Trinkler, H. 1968. Working with Formaldehyde. Med. Lab. 21(12): 283-290 (Ger).

D-4. Medical technicians, cleaning personnel, and textile workers having contact with HCHO (presumably formalin solutions as well as vapors) reported eczema, throat pains, coughing, and asthma-like diseases. No HCHO levels or length of employment given.

5-108 Trubitskaya, G. P. 1978. Chemical Air Pollution in Furniture Stores. Kazan. Md. Zh. 59(1):81-82 (Russ).

C-5. Furniture store workers and the persons living in apartments above the store were exposed to 0.116-0.324 mg HCHO/m^3 and 0.007-0.046 mg HCHO/m^3 respectively. Complained of headaches, difficulty breathing, and irritation of the mucous membrane of the eye. Essentially a small, uncontrolled, descriptive study.

5-109 Trubitskaya, G. P., A. N. Boiko, R. F. Komarova, and N. P. Cherednichenko. 1978. Effect of a Low-Intensity Chemical Factor on Children Under Conditions of the Use of Polymeric Materials in Construction. Pediatriya (Moscow) No. 8:26-29.

D--. Children, 2- to 7-y-old, in a school constructed of nonpolymeric materials where the concentrations of HCHO, phthalates, and NH_3 were 0.006-0.016 (avg. 0.010), trace, and 0.046-0.129 (avg. 0.092) mg/m^3, respectively, suffered significantly fewer cases of allergic reactions and sicknesses such as exudative diathesis, nettle rash, and reactions to medicine than similarly aged children in two schools constructed of polymeric materials. In the latter two schools, the concentrations were HCHO, 0.008-0.027

(avg. 0.010) and 0.009-0.032 (avg. 0.017) mg/m^3; phthalates, trace and 0.048-0.079 (avg. 0.055) mg/m^3; and NH_3, 0.046-0.268 (avg. 0.124) and 0.057-0.224 (avg. 0.134) mg/m^3.

5-110 Tuazon, E. C., R. A. Graham, A. M. Winer, R. R. Easton, J. N. Pitts, Jr., and P. L. Hanst. 1978. A Kilometer Pathlength Fourier-Transform Infrared System for the Study of Trace Pollutants in Ambient and Synthetic Atmospheres. Atmos. Environ. 12(4):865-876.

C--. Ambient air at Riverside, California, during August-October 1976 contained ppb concentrations of HCHO, HCO_2H, NH_3, and other trace contaminants.

5-424 Urban, C. M., and R. J. Garbe. 1980. Exhaust Emissions from Malfunctioning Three-way Catalyst-equipped Automobiles. SAE Tech. Pap. Ser. 800511. 11 pp.

C--. Maximum emission rates (mg/m^3) in 4 malfunctioning, 3-way catalyst-equipped automobiles:

NH_3	254
CN-	67
H_2S	8
HCHO	3

5-167 USA Standards Committee on Acceptable Concentrations of Toxic Dusts and Gases, Z237. 1967. USA Standard Acceptable Concentrations of Formaldehyde. USAS Z37.16-1967, United States of America Standards Institute, New York, New York. 8 pp.

C--. The acceptable workplace concentration selected to avoid discomfort is 3 ppm (TWA) with 5 ppm as an acceptable ceiling limit.

5-304 USDA, U.S. Department of Agriculture, Forest Service. 1977. The Formaldehyde Problem in Wood-Based Products--An Annotated Bibliography. USDA Forest Service Gen. Tech. Rep. FPL-8, Forest Products Laboratory, Madison, Wisconsin. pp. 47-57.

C--. The section on the toxicology of HCHO contains ~ 45 citations, not all of which are annotated.

3-094 U.S.S.R. State Committee of the Council of Ministers for Construction. 1972. Sanitary Norms for Industrial Enterprise Design. Publishing House of Literature on Construction, Moscow. 96 pp. (Russ).

C--. In the U.S.S.R., the MAC for HCHO in workplaces was 0.5 mg/m^3, and in populated places was 0.035 mg/m^3 for a one-time and 0.012 mg/m^3 for a mean diurnal level.

5-413 Van Gemert, L. J., and A. H. Nettenbreijer. 1977. Compilation of Odour Threshould Values in Air and Water. National Institute for Water Supply. Leidschendam, The Netherlands, and Central Institute for Nutrition and Food Research, TNO, Zeist, The Netherlands.

A--. Compilation of odor threshold values reported by different researchers, for many compounds, including:

NH_3	0.03 - 37 mg/m^3
HCN	< 1.1 - 6
H_2S	0.001 - 2
HCHO	0.033 - 2.2
Methanol	4.3 - 11,700
Acrolein	0.05 - 4.1

5-384 Vernon, T. M., S. W. Ferguson, and T. A. Edell. 1978. Formaldehyde Vapors Create Health Problems. Colorado Bull. 6(51):1.

C--. This bulletin recommends that elderly persons and those with chronic respiratory disease be warned that HCHO vapors may be hazardous to their health, that persons with allergies should be warned that HCHO exposure may aggravate existing symptoms and/or precipitate new allergies. Avoidance of HCHO exposure is recommended for pregnant women, infants, and children. The report states that chronic nausea, vomiting, and diarrhea in infants and young children living in homes insulated with urea-HCHO have been reported.

5-276 Vinogradov, G. I., and M. I. Rudnev. 1976. Immunological Reactivity to the Effect of Carbon Monoxide and Formaldehyde in the Air. Gig. Sanit. No. 9:9-12 (Russ).

B-7. HCHO poisoning (0.011 mg/m^3 for 21 d) led to an increase in the immunobiological reactivity of the exposed guinea pigs. However, subsequent stress, in the form of hypoxia, caused a sharp depression of all the studied indexes in contrast to the controls, revealing the inferior resistance of the test animals.

5-275 Vinogradov, G. I., I. A. Chernichenko, and E. M. Makarenko. 1974. Allergic Activity of the Motor Traffic Exhaust Gas. Gig. Sanit. No. 8:10-13 (Russ).

B-7. Exposure of guinea pigs to HCHO at 0.011, 0.038, or 0.38 mg/m^3 for 21 d was accompanied by injury to the neutrophils, degranulation of the basophiles, and increase in the titer of antibodies in bound complement. The results confirm the sensitizing action of HCHO.

5-015 Volkova, Z., and E. Sidorova. 1971. Formaldehyde Content in Blood of Persons Working in Contact with Urea-Formaldehyde Resins. Gig. Tr. Prof. Zabol. 15:44-46 (Russ).

C-9. Concentrations of HCHO in the blood of workers was positively correlated with the degree of exposure via inhalation and skin contact. By the start of the next day, only the most heavily exposed workers contained HCHO in the blood, and this may have been due to contamination of the clothing they wore home. HCHO concentrations in the workplace air ranged from 0.31 to 8.8 mg/m^3; in the blood of exposed workers at the end of the day, from < 0.06 to 0.70 mg %.

5-387 Von Oettingen, W. F. 1958. Poisoning. A Guide to Clinical Diagnosis and Treatment. 2nd ed., W. B. Saunders Co., Philadelphia, Pennsylvania. p. 365.

C--. This very brief summary of HCHO toxicity by inhalation, dermal, or oral routes mentions that following ingestion of HCHO and its expected direct action on the gastrointestinal tract, there may be diarrhea, tenesmus, anuria, and injury of the liver.

5-277 Wallenstein, G., and E. Rebohle. 1971. Results of Experiments on Allergic and Irritative Effects of Formaldehyde on the Respiratory Tract. Z. Erkr. Atmungsorgane 135(3):359 (Ger).

C-7. Of 78 patients exposed to HCHO-containing resins on their jobs who exhibited respiratory sensitivity to HCHO--vasomotor rhinitis, chronic bronchitis, and obstructive respiratory problems--only 17% showed a positive reaction to epicutaneous exposure and 5% showed a positive late reaction to the intracutaneous test. Sixty-two percent showed a nonspecific bronchial hyperactivity (positive acetylcholine test). No inhalation provocation tests were done. There were workplace exposure values for only 7 cases--5-25 mg/m^3, which exceeded the MAC of 3 mg/m^3.

5-278 Wallenstein, G., and E. Rebohle. 1976. Sensitization to Formaldehyde in Occupational Exposure by Inhalation. Allerg. Immunol. 22(3):287-290 (Ger).

D-5. Determinations of skin test sensitivity to HCHO of workers in various industries with HCHO exposure. 22/180 (12.2%) showed positive sensitization. Of these, none showed a clear positive response to provocative tests (nasal and inhalation application). No environmental sampling was done to correlate exposure to test results.

5-303 Wanner, H. U. 1978. Hygienic Evaluation of the Pollutants from Living Room Air. In: Org. Verunreinig. Umwelt: Erkennen, Bewerten, Vermidern, [Tag.]. K. Aurand, V. Haesselbarth, E. Lahmann, G. Muller, and W. Niemitz, Eds. Erich Schmidt Verlag, Berlin, Germany. pp. 405-415 (Ger).

C--. A review of CO, HCHO, acrolein, and N oxides in indoor air. In 1978, Satish and Wanner found HCHO concentrations of 32-46 ppb in indoor air in the winter (6-8 ppb outdoors) and 48-124 ppb in indoor air in the summer (13-15 ppb outdoors).

5-115 Wanner, H. U., A. Deuber, J. Satish, M. Meier, and H. Sommer. 1977. Evaluation of Air Quality in Streets. Proc. Int. Clean Air Congr., 4th, Tokyo, Japan. pp. 551-554.

C--. HCHO concentrations in ambient air at outdoor sites varied little with wide differences in traffic density (9.3-12 ppb), but indoor air concentrations were considerably higher: traffic canyon first floor office, 85 ppb; suburban apartment, 53 ppb; and residential area "store and dispatch," 41 ppb.

5-016 Wayne, L. G., R. J. Bryan, and K. Ziedman. 1976. Irritant Effects of Industrial Chemicals: Formaldehyde. Publ. No. 77-117. National Institute for Occupational Safety and Health, Center for Disease Control, Public Health Service, U.S. Dept. of Health, Education, and Welfare, Cincinnati, Ohio. 135 pp.

B-9. HCHO levels were determined in garment apparel workshops and wood products plants, but health effects were evaluated in only one--a large wood products plant. No significant relations between HCHO exposure and eye disorders, irritation symptoms, or visual function were observed.

5-348 Weber, A., C. Jermini, and E. Grandjean. 1976a. Irritating Effects on Man of Air Pollution Due to Cigarette Smoke. Am. J. Public Health 66(7):672-676.

D-11. Exposure is confounded for the purposes of this task, but worth a mention as an interaction study with HCHO and acrolein as probably the primary irritants. The sidestream smoke from 30 cigarettes added to a 30 m^3 room for 26 min resulted in ~ 71 ppm CO, ~ 1.32 ppm HCHO, and ~ 0.30 ppm acrolein. The results of self-rated intensity of eye irritation paralleled the increases in irritants with time. Nose and throat irritatation, respiratory and general complaints, and poor air quality judgements also increased with time, although weaker and less obviously paralleling irritant concentration. Nonsmokers were slightly more sensitive.

5-280 Weber, A., T. Fischer, E. Sancin, and E. Grandjean. 1976b. Air Pollution Due to Cigarette Smoke: Physiological and Irritating Effects. Soz.-Praeventivmed. 21(4):130-132 (Fre.).

D-4. A group of 33 subjects was exposed to an increasing concentration of cigarette sidestream smoke for 28 min. (containing 0.03-0.64 ppm HCHO, 1-43 ppm CO, 0.08-1.5 ppm NO, and 0-0.2 ppm acrolein). Eye irritation and subjective annoyance (the more sensitive criterion) increased with time, smokers and nonsmokers apparently equally sensitive. No significant differences in lung function were observed.

5-281 Weber-Tschopp, A., C. Jermini, and E. Grandjean. 1976c. Air Pollution and Irritation Due to Cigarette Smoke. Soz.-Praeventivmed. 21(2-3):101-106 (Ger).

D-11. The same data are reported in Weber et al. (1976a) [5-348].

5-279 Weber-Tschopp, A., T. Fischer, and E. Grandjean. 1976d. Physiological and Psychological Effects of Passive Smoking. Int. Arch. Occup. Environ. Health 37(4):277-288.

D-11. Apparently the same study as Weber et al. (1976b) [5-280], but with more experimental detail given. Superseded by Weber et al. (1976a) [5-348], a larger study with more subjects.

5-117 Weber-Tschopp, A., T. Fischer, and E. Grandjean. 1977. Irritating Effects of Formaldehyde (HCHO) on Men. Int. Arch. Occup. Environ. Health 39(4):207-218 (Ger); English translation by M. Tandy, Health and Safety Executive Library and Information Service.

A-15. Comparison of exposure to continuously increasing HCHO levels (0-3.2 ppm) for 37 min and repeated 1.5-min exposures to 1, 2, 3, or 4 ppm. Adaptation occurred in the 1st instance, and all values of irritation and distress were lower than those for repeated exposures to 2-4 ppm. Overall, the avg. threshold of irritation for HCHO was 1-2 ppm. Therefore, the authors recommend a TLV of < 2 ppm.

5-298 Weiss, H., M. A. Woodbury, and W. Taylor. 1981. Risk Factors and Infant Mortality; A County Study with an Emphasis on Dwelling Type. Abstract of Paper Submitted March 5, 1981, to the American Public Health Association 109th Annual Meeting, Los Angeles, California, November 1981; and personal communication from H. Weiss to B. L. Carson, March 19, 1981.

D-6. This study, based on analysis of death certificates, confirms a preliminary report that there is an increased risk of infant mortality among mobile home residents (23.4% mortality) vs. non-mobile home residents (13.3%) in Eau Clair County, Wisconsin. However, the results tend to show only that mothers living in mobile homes are younger and less educated so that the twofold greater incidence of infant mortality is merely that expected from mothers of a lower socioeconomic class. The study does not look specifically at newer mobile homes where HCHO emanations would be expected. In fact, there are no HCHO measurements at all.

5-203 Williams, J. E., and C. D. Gordon. 1970. The Hatchability of Chicken Eggs Fumigated With Increasing Levels of Formaldehyde Gas Before Incubaton. Poultry Sci. 49(2):560-564.

D-11. Exposure of eggs before incubation to ~ 0.5 to 2.5 mg HCHO/m^3 for 20 min. Number of chicks hatched was reduced slightly, more so in brown eggs and eggs from older hens.

5-282 Wynder, E. L., D. A. Goodman, and D. Hoffmann. 1965. Ciliatoxic Components in Cigarette Smoke. II. Carboxylic Acids and Aldehydes. Cancer (Philadelphia) 18(4):505-509.

C-8. The methods of this clam gill cilia study are not fully described. The lowest level of HCHO tested was 0.05% (500 ppm) and this produced almost immediate complete stasis of ciliary activity with eventual recovery. 0.1-1.0% (1,000-10,000 ppm) acrolein caused immediate and complete ciliastasis, while 0.05% (500 ppm) caused immediate loss of metachronic wave in the lateral cilia and partial stasis at ~ 1 min with no further effect.

5-119 Yamate, N., T. Matsumura, T. Inoue, and E. Higuchi. 1978. Summary of Air Pollutant Levels at Three National Auto Exhaust Monitoring Stations in Tokyo in 1977. Eisei Shikensho Hokoku No. 96, 119-123 (Japan); Chem. Abstr. 1979. 91:111832w.

C--. HCHO concentrations measured at the gas monitoring stations declined from 0.01 ppm in 1969 to 0.006 ppm in 1977.

5-172 Zaeva, G. N., I. P. Ulanova, and L. A. Dueva. 1968. Materials [Information] for Revision of the Maximal Permissible Concentrations of Formaldehyde in the Interior Atmosphere of Industrial Premises. Gig. Tr. Prof. Zabol. 12(7):16-20 (Russ); English translation available from John Crerar Library, Chicago, Illinois. Order No. 74-13625-06J.

B-5. A review of the Russian literature, the authors recommending a maximum permissible concentration in the air of workplaces of 0.5 mg HCHO/m^3.

5-173 Zannini, D., and L. Russo. 1957. Consequences of Acute Intoxications Due to Gaseous Irritants of the Respiratory System. Lav. Um. 9:241-253 (Ita); English translation available from John Crerar Library, Chicago, Illinois. Order No. 75-21078.

C-5. Of 18 persons acutely poisoned by gaseous irritants, only one had been exposed to HCHO (no concentrations given). This 40-y-old person complained of dyspnea on exertion, asthma attacks, weight loss, and nervousness. Chest showed harsh respiration and disseminated rhonchii. The left side of the heart was enlarged. There was accentuation of the 2nd pulmonary tone on the pulmonary focus, and the thyroid was hypertrophic. Vital capacity and max. pulmonary ventilation had decreased 40 and 45%, respectively. The decrease in diaphragm motility may have been attributable to loss of general condition due to rest at home as well as to bronchopulmonary lesions.

5-121 Zitting, A., and H. Savolainen. 1979. Neurotoxic Effects of the Oxidative Thermal Degradation Products from Low Density Polyethylene. Fire Mater. 3(2):80-83.

C-10. Repeated exposure of rats to polyethylene combustion products containing 1.4 ppm HCHO, 0.5 ppm acrolein, ash, CO, and mixed aldehydes for 6 h/d, 5 d/wk for 2-5 wk led to undesirable neural effects.

APPENDIX A

HUMAN STUDIES IN PROGRESS

A "Review of Planned and On-Going Epidemiological Studies of Formaldehyde," excerpted from the Report of the Federal Panel on Formaldehyde (Griesemer et. al., 1980) is included in this Appendix.

MRI contacted by letter many of the principal investigators of these on-going studies, and those complete or near-complete reports received in reply were included in the preceding chapters. To correlate the information received with the remarks concerning each study by Griesemer et al. (1980), we have identified each study by the numbering system used in the excerpt.

"II.a)" This is presumably the report by Giulietti (1980), which is included in Table V-2.

"II.b)" The report of Marshall (1980) is included in Table V-2.

"II.c)" No response.

"III.a)" Following written and telephone inquiries, MRI was told that information on Dr. Levine's studies was not available.

"III.b)" The report of Thun et al. (1980) is included in Table V-2.

"III.c)" No data are available yet for Woodbury and Zenz's study of new mobile home owners. The last samples were to have been collected in May 1981 (personal communication to B. L. Carson from Mary Ann Woodbury of the Wisconsin Department of Health and Social Services, January 1981). The results on the retrospective study of 65 mobile home residents are discussed in Hanrahan et al. (1980?) and the data given in Table V-2.

"III.d)" Dr. Williams' study, "Survey of Mobile Home Residents in Two Different Coastal Regions: Coastal and Inland," had obtained answered questionnaires but no funding for data analysis. Formaldehyde measurements were not made (personal communication to Dr. H. V. Ellis, III, from Dr. L. P. Williams of the Office of State Health Division, Department of Disease Monitoring and Control, Oregon, December 1980).

"IV.a)" No letter sent.

"IV.b)" Data collection for Dr. Grauman's study of medical technologists was not scheduled to begin until March 1981. The report was estimated to be completed in mid-1982. Dr. Graumann is working on a similar study of 5,000 histotechnologists, with greater exposure levels. A preliminary report may be ready by October 1981, to be given at the National Histotechnologists meeting (personal communication to Dr. Ellis from Dr. Dan Grauman, National Cancer Institute, December 1980).

"IV.c)1)" Results of Dr. Walrath's study are given in a paper presented at the C.I.I.T. Conference on Toxicology: Formaldehyde Toxicity (received from Dr. Walrath in January 1981), and described in Table V-1.

"IV.c)2)" A protocol for the California embalmers study was received from Dr. Walrath in January 1981, but no data have been collected.

"IV.c)3)" Following written and telephone inquiries, MRI was told that information on Dr. Levine's studies was not available.

"IV.d)" The first phase of finding a suitable cohort has apparently been undertaken by Westat, Inc. (Anonymous 1980b). Several reservations about the proposed course of study have been made by Dr. Irving Selikoff of Mt. Sinai Medical Center (Anonymous, 1980a). A request-for-proposal has been issued for a mortality study of the 5,000-10,000 worker cohort (Anonymous, 1981b).

Two additional on-going studies were found which are not discussed in Griesemer et al. (1980). Dr. Genevieve M. Matanoski is conducting a study of pathologists, originally investigating the virological risk but later broadened to consider the possible influence of past formaldehyde exposure on mortality. To date, the data indicate a significant increase in mortality due to liver cancer, some excess of kidney cancer, and a lower relative risk of oral pharyngeal carcinoma (Matanoski, 1980). Richard Dailey is the project officer for a study entitled, "Integrated Risk Assessment of Formaldehyde," sponsored by the Interagency Regulatory Liaison Group.

The following pages in this Appendix were copied directly from the Report of the Federal Panel on Formaldehyde (Griesemer et. al., 1980). This page lists all of the panel members and their affiliations.

Panel Members

Richard A. Griesemer*, D.V.M., Ph.D. (Chairman)
National Cancer Institute

Andrew G. Ulsamer, Ph.D. (CPSC Liaison)
Consumer Product Safety Commission

Joseph C. Arcos, Ph.D.
Environmental Protection Agency

James R. Beall, Ph.D.
Department of Energy

Aaron E. Blair, Ph.D.
National Cancer Institute

Thomas F. X. Collins, Ph.D.
Food and Drug Administration

Federick J. de Serres, Ph.D.
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National Cancer Institute

Elizabeth K. Weisburger, Ph.D.
National Cancer Institute

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* Now at the Oak Ridge National Laboratory.

Review of Planned and On-Going Epidemiological Studies of Formaldehyde

Planned and on-going investigations related to formaldehyde exposure include one study of a new technique of measuring formaldehyde, three studies investigating complaints, four epidemiological studies of morbidity (cross-sectional and prospective), and six mortality studies (cohort, proportionate mortality, and case-control). The questions being addressed and an evaluation of each group of studies follows.

I. Measurement Technique

The use of solid absorbent surfaces for collecting personal samples of vapor and particulate formaldehyde is being examined. This method should be more sensitive and efficient than the present impinger method, thereby permitting more accurate assessment of environmental exposures. An occupational study (cross-sectional morbidity) is planned, but details have not yet been provided.

II. Investigation of Complaints Relating to Formaldehyde

The results from three states are being compiled:

a) In Connecticut persons complaining of health problems due to urea-formaldehyde insulation completed a questionnaire concerning their symptoms and air levels of formaldehyde were measured in their homes. Occupants 489/794 of 262 residences presented complaints, the most common symptoms being eye, nose, and throat irritation, and headaches. Formaldehyde concentrations ranged from 0 to 10 ppm (mean of 1.5 ppm). About 1/2 of the complaints were associated with levels of 1/2 to 10 ppm.

b) F. Marshall of the New Jersey Department of Health obtained medical histories, all available information on insulation, and patterns of health effects from residents with recently installed urea-formaldehyde foam insulation who complained of formaldehyde odor, irritation, or increased pre-existing illness patterns. In 40/55 homes investigated, the most common symptoms were tearing of the eyes, sore throat, cough, and runny nose. Air samples were collected in 22 homes. In 14 homes where formaldehyde was detected, levels ranged from .01 to 0.78 ppm.

c) In New Hampshire, the Bureau of Occupational Health (M. Hilgemeier) administered a standard questionaire to residents with complaints associated with formaldehyde exposure. Standard NIOSH techniques were used to collect formaldehyde samples. About 90% of the samples were below 0.5 ppm; 10/77 dwellings were mobile homes.

The above studies on formaldehyde complaints are all similar and suffer the same deficiencies. None of them can be used to estimate prevalence of symptoms nor can they be used to establish dose-response relations. These shortcomings include: 1. The surveys are conducted only among those who complain, and although the prevalence of symptoms should be high, it is a biased sample; 2. There are no controls and no measurement of other irritants that could cause health complaints. Thus, these studies are only suggestive of possible problems and by themselves provide little evidence of cause and effect relationships.

III. Morbidity

The following studies are underway:

a) R. Levine of the Chemical Industry Institute of Toxicology studied approximately 100 West Virginia morticians in a cross-sectional study of lung function (spirometry) and respiratory symptoms. Employment and smoking histories were also obtained. Industrial hygiene measurements made in the mortality study of Ontario embalmers along with symptoms during embalming, number of bodies embalmed, subjective assessment of severity of fumes, and length of employment will be used to assist in the estimation of exposure in this study. Spirometry will be compared to predicted values from Knudson, and internal comparisons will be related to exposure after age, height, and smoking adjustments.

Data from this study are being analyzed in terms of the prevalence of respiratory symptoms (cough, phlegm, dyspnea) and the relation of percentage of predicted pulmonary function to employment (formaldehyde exposure) after adjustment for confounding variables. There is no assessment of skin effects. It is not clear if acute symptoms related to exposure are to be evaluated.

Although there is a good rationale for studying this occupational group, an inability to detect a significant response in this study could be due to low cumulative exposure (probably less that 8 hours/day). Length of exposure (years worked or latency) should be adequate. If we assume 50 persons each (smoking groups combined) in a high and low exposure group (the optimal situation) there is an 85% chance of correctly rejecting the null hypothesis of no difference in FEV between exposure groups, if the true difference is 0.5 liters and α level is 5%. If the symptom rate is 20% in the low exposure group, there is less than a 50% chance of correctly rejecting the hypothesis of no difference if the true difference is 20% at the 5% α level (two-tailed test). As in all cross-sectional studies, estimates of exposure are only a crude indicator of actual exposure. This is, however, one of the few studies to attempt to assess long term effects of formaldehyde on lung function. Although embalming fluid contains 1-2% formaldehyde, other pulmonary irritants are also present (e.g., phenol) but these may be at low enough concentrations to have a minimal effect. A comparison group (e.g., funeral directors) would have provided more confidence in the results and more power in the analysis.

The remaining three morbidity studies are of residents in homes with urea-formaldehyde (UF) foam insulation.

b) M. Thun of the New Jersey Department of Health identified about 400 homes that had been insulated with UF foam and an equal number of control homes. Information gathered by telephone interview included type of home and insulation, formaldehyde odor, health symptoms and other medical data, demographic data on the occupants, and the period prevalence of asthmatic attacks, wheezing, chest pain, stinging or burning skin,

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burning or tearing eys. Except for wheezing, the controls reported a higher prevalence of symptoms than did UF foam households. There was no detectable difference in the overall incidence of new symptoms during the year. There was, however, an association of increased symptoms and formaldehyde odor; the incidence of new symptoms following installation of the insulation was 2.7 times higher than in the months preceding the insulation. About 64% of the residents of the UF foam homes reported no problems at all related to the foam insulation. There is the possibility of selective recall in the remaining 36% of the study group because of the possible publicity relating to mobile homes and the specific questions relating to insulation. Despite this potential bias, there was little overall difference between study and comparison populations. There was however, a dose-response relation (dose was based on odor). Unfortunately, there were no environmental measurements to correlate with odor perception and symptoms, and appararently no control of other potentially confounding irritants other than formaldehyde. The added insulation may have also increased other respiratory irritants that could have raised the symptom rate. It is not clear how the formaldehyde odor was described to the subjects. This study has been completed recently and should be available for review shortly. The summary given the Panel suggests little difference between the insulated and control homes except when odor occurred.

c) M. Woodbury and C. Zenz of the Wisconsin Department of Health and Social Studies are proposing to study 110 new mobile home owners. Exposure measurements are to be made twice monthly for 9 months.

It is difficult to evaluate this prospective study because of the lack of detail provided. Some of the questions that need answering are:

- What are the health parameters that will be determined and how often are they being monitored?
- Are there formaldehyde controls for the mobile homes? If so, how are they selected? If no controls are planned, the study will have limited value.
- Are other respiratory irritants being measured (e.g., NO_2)?

About 50%of the homes are newer homes with higher formaldehyde levels than the older homes which are serving as controls and have measurable but low levels of formaldehyde. Assuming a 20% symptom rate and 180 people in each exposure group (high and low formaldehyde), there is about an 35% chance of correctly rejecting the hypothesis of no differences in symptoms when the true difference is 15% at the 5% α level, and about a 99% chance of correctly rejecting the hypothesis of no difference in FEV, when the true difference is 500 mL at the 5 % α level (two-tailed test). The effects of long-term chronic exposure cannot be estimated by this study.

These investigators also performed a retrospective pilot study of 65 mobile home residents. The data will be mainly useful in the planning and execution of the prospective study.

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d) L. Williams of the Oregon Department of Disease Monitoring and Control is planning to study 300 mobile home residents who responded to a health questionnaire. The volunteers were from two regions, coastal and inland. The purpose of the study is to ascertain the effect of humidity, temperature, and wind ventilation on "health effects to potential formaldehyde exposure."

Inasmuch as the participants in the study are volunteers, however, it is not a random sample. Apparently, environmental measures are planned, but it is not known what other information on insulation, demography, other pulmonary irritants, humidity, temperature, etc., will be collected. Although the details are unknown, this study design does not promise to add very much to our knowledge. The power in this study is similar to the study by Woodbury and Zenz when the following assumptions are made:

1) the two exposure groups to low and high formaldehyde are of equal size (∼ 150);

2) the prevalence of symptoms is about 30% in low exposure group.

IV. Mortality

a) H. Weiss of the Wisconsin Department of Health and Social Sciences conducted a case-control study of infant mortality by type of residence and found an increased risk for mobile home residents. Socioeconomic status is only one of many sources of potential bias in this study. The completed study should be reviewed, but the short description available suggests that the data will provide little, if any, useful information on the effect of formaldehyde.

b) D. Grauman of the National Cancer Institute proposes to evaluate the mortality experience (using standardized mortality ratios [SMR] of a cohort of about 11,000 medical technologists. This group is exposed to other chemicals in addition to formaldehyde (e.g., chloroform and benzidine). No environmental data are available, so there cannot be a good estimate of exposure-response relationships. A positive association will not be conclusive because of the mixed exposure. A negative association will not be conclusive because of the lack of exposure information and the possibility of low exposures. The control group is to be the U.S. population. If 15% of the cohort are dead (n = 1650 cases) and if 20 % of the deaths in the control population were from cancer, there would be better than a 95% chance of correctly rejecting the hypothesis of no difference between exposed and controls if the true differences were 5% at the 5% α level. Assuming 1/4 of all cancers were lung cancer, there is about an 80% chance of correctly rejecting the hypothesis of no difference if the true differences were 5% at the 10% α level (two-tailed test).

c) There are three mortality studies of embalmers.

1) J. Walrath is conducting a proportionate mortality ratio analysis of about 1500 morticians from New York. The purpose is to determine whether there is an excess proportion of deaths due to specific malignant neoplasms compared to the general population. Besides having the problems inherent in a PMR analysis where the population-at-risk is not available there is little exposure data (length of exposure is estimated on the basis of the year first licensed). Assuming the rate of lung cancer is 5%, there is better than a 99% chance of correctly rejecting the hypothesis of no difference in lung cancer rates when the true difference is 5% at the 1% α level (two-tailed test).

2) Dr. Walrath is conducting another PMR study on about 1200 embalmers from California. This study is very similar to the one in New York, except there will be more information on length of exposure which can be evaluated. There is, however, no direct estimate of exposure or smoking history or other confounding exposures. If 20% of the deaths were from cancer, there would be a better than 90% chance of correctly rejecting the hypothesis of no difference in cancer rates between exposed and controls if the true differnces were 5% at the 10% α level (two-tailed test).

3) R. Levine of the Chemical Industry Institute of Toxicology is also studying embalmers using an SMR retrospective mortality design. The cohort is composed of Ontario's funeral service professionals licensed during 1914-1967. Date of birth, date of first licensure, type of license, years licensed, and place of employment are available for each person. Observed mortality rates will be compared to Canadian national and provincial mortality data. Mortality will also be analyzed as a function of exposure (years worked ?). A retrospective industrial hygiene assessment will consist of inquiring about changes in funeral practices with time, surveying several selected funeral establishments. The survey will include air sampling for agents of potential health concern (e.g., formaldehyde, phenol) and examination of purchase records to determine amount and kind of chemicals used. Presumably these data are to be used in evaluating dose-response relationships. Assuming the study population comprises 180 deaths (15% of the estimated cohort) and a 20% cancer rate there is about a 50% chance of correctly rejecting the hypothesis of no difference if the true difference is 10% at 5% α level (or an 85% chance if the true difference is 15% at the 5% α level).

As a group, these three studies of embalmers should provide a good estimate of potential risk from formaldehyde exposure.

d) A. Blair at NCI and the Formaldehyde Institute are collaborating on a proposed cohort mortality study to develop age, race, and sex-specific mortality rates among formaldehyde-exposed workers. Rates will be compared with those in the U.S. population and local or regional populations where appropriate.

The first phase of the investigation is to determine if there is a suitable cohort for study. Suitability will be based on representatives of the participating companies, range of exposure, availability of a cohort of at least 3,000 workers with a minimum 15-year latent period, suitable age distribution, and sufficient information for adequate follow-up. If the requirements for a scientifically sound study are met, the study will proceed. Formaldehyde exposure for each individual will be estimated using job titles, work locations, past environmental measurements, years of employment, and the presence of potentially confounding exposures. The exposed group will be stratified by intensity and duration of exposure, age and year of first exposure, susceptibility, and latency.

The cohort should be large enough to engender confidence in the differences in mortality experience of study and comparison populations. Although exposures are unlikely to be to pure formaldehyde, because of the varied occupational exposures and size of the cohort, it may be possible to assess the individual contribution of formaldehyde. Although the assessment of exposure is retrospective, it can still be at least semi-quantitative. This is a very important part of this study and should employ a full-time industrial hygienist following methods similar to those of Emsden at the University of Pittsburgh. It is important that all companies participate in the study, as the results may be seriously biased if some do not.

Conclusions

Of all the mortality studies proposed, those examining the medical technologists, embalmers, and formaldehyde workers are the only ones that can assess the carcinogenic risk among those individuals exposed. Although single epidemiologic studies usually cannot adequately assess an occupational risk, or the risk of exposure to a chemical agent, taken together these studies should help clarify the situation. There are, however, a number of concerns about these studies including:

a) Are exposures to formaldehyde high enough in these populations to assess possible effects? For example, are embalmers exposed 8 hours/day, 5 days/week, or is their exposure much less?

b) Can exposure history be adequately documented?

- Are individuals with little or no embalming experience distinguishable from those with considerable exposure?
- Since few if any of the workers are exposed only to formaldehyde, what is the effect of exposure to these other agents?

c) Is exposure to formaldehyde in the same range as for other populations?

The confidence we place in the findings from these studies depends largely on the ability to retrospectively estimate exposure. If exposure in these occupational groups is representative of other exposed populations, the conclusions may be indicative of potential risk to all exposed populations. If these studies do not adequately address the above questions, then further investigation may be required. Such investigation may be pursued within the existing data set, or new populations may need to be investigated.

Recommendations for Epidemiologic Research

There is a need for carefully designed epidemiologic studies to evaluate the role formaldehyde may play in the origin of certain chronic diseases. Specific research areas identified by the Panel include:

1. Additional studies of chronic respiratory system disorders that include environmental measurements to allow a more precise estimate of risk at various exposure levels. These should include industrial, as well as mobile home populations.

2. Projects designed to confirm or deny the association of menstrual and reproductive disorders and formaldehyde exposure reported by Shumilina (1975).

3. More complete epidemiologic studies to evaluate the carcinogenicity of formaldehyde in human populations. Although several projects are under way, there is a need to be alert for resources for additional research. The widespread use of formaldehyde in industry and its occurrence in a variety of consumer products may provide opportunities for other studies. The many uses of formaldehyde are summarized in the NIOSH Criteria Document (1976) and will not be itemized here. It is sufficient to say that the chemical is of importance in adhesives for particle board and plywood production; resins to mold a variety of plastic parts for automobiles, appliances and hardware; wrinkle-resistance in textile manufacturing; strengthening of various paper products (grocery bags, wax paper, napkins and tissues, and filter paper); specimen preservation; mildew prevention; insulation; and protective coatings.

It may be possible to identify other formaldehyde-exposed cohorts for study. The major difficulty is that, for most occupations or industries, only a small proportion of the workers have actual contact with formaldehyde. This is clearly demonstrated from the NIOSH Occupational Hazard Survey, Phase I, 1972-1974, where 4,636 plants were studied in over 600 different industry types (according to S.I.C. codes). These plants employed 895,725 workers in 453 different occupations. Products containing formaldehyde were encountered in 396 separate S.I.C.-coded industries. The following list gives the percentage of workers exposed to formaldehyde in the industries with the larger work forces, and those of particular interest.

Industry	% of Workers Exposed
Medical	
Veterinarian and animal hospitals	23.0
Funeral Services	100.0
Medical laboratories	31.0
Construction	
Forestry services	10.5
General building contractors	3.6

Heavy construction	3.7
Plastering and lathing	5.4
Textiles	
Finishing plants (synthetics)	11.6
Coated fabrics	14.0
Hats and caps	47.0
Fabricated textile products	3.3
Wood and Paper	
Veneer and plywood	21.0
Wood products	8.6
Upholstered furniture	12.2
Paper mills	5.8
Paper coating and glazes	9.0
Bags (except textiles)	11.1
Paints and allied products	16.9
Fabricated rubber products	29.0
Abrasive products	11.0

This survey confirms an impression given by published reports that exposure to formaldehyde is more common in medical and laboratory environments and in certain parts of the textile, wood, and paper industries. In certain industries, however, the number of work places and workers studied was small and the survey may not have included those where significant exposure to formaldehyde occurs (e.g., the chemical manufacturing industry).

The Industry-wide Studies Branch of NIOSH is carrying out an industrial hygiene study of formaldehyde exposure in several industries in search of a suitable cohort for a mortality study of formaldehyde exposed workers. Measurements will be made in industries concerned with formaldehyde manufacture, textile and clothing production, wood furniture and wood and paper product manufacture. Fifteen site visits are planned and these will be completed over the next six months.

The major difficulty of the mortality studies of individuals exposed to formaldehyde is the limited ability of such studies to detect excess risk for rare causes of death. Since the known carcinogenic action of formaldehyde is limited to the nasal sinuses in rats, there is a need to evaluate the risk for this site in man, although it is clear that carcinogens may not affect the same tissues in humans as in laboratory animals. It is unlikely that a cohort of sufficient size can be assembled to accomplish this task; however, a carefully designed case-control study might. The Panel suggests that the feasibility of performing a case-control study of cancer of the nasal sinuses in areas where there is heavy production or use of formaldehyde as a vapor should be explored.

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